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CONTENTS

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OUR JOURNAL IS TWENTY YEARS OLD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 24 Oct 86) pp 4-9

[Article by O. G. Gazenko, A. A. Gyurdzhian and A. A. Shipov]

[English abstract from source] This review describes the history of the journal--its establishment and development associated with the advances in space biology and aerospace medicine. The paper summarizes the major areas of research discussed in the publications and emphasizes their relations with other branches of science. It also lists readers' comments, suggestions and recommendations derived from the recent questionnaires. The paper outlines the objectives of the journal as related to further development of space biology and aerospace medicine.

[Text] In 1987, the 70th anniversary of the Great October Socialist Revolution, the journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, will be 20 years old.

In 1967, a large detachment of scientists, physicians and biologists, physiologists, hygienists and psychologists, engineers and designers concerned with medical and psychological support of space and aviation flights, development of life-support and flight-safety systems, designing models of biological and physiological processes, and people interested in development of the fundamental bases of space biology and aerospace medicine acquired a platform for exchange of knowhow, scientific discussion and publication of results of experimental research in the form of the journal, KOSMICHESKAYA BIOLOGIYA I MEDITSINA [Space Biology and Medicine].

As we know, a specialized scientific periodical plays the role of a center for scientific communication between researchers working in the same or allied fields, and it reflects to a significant extent the dynamics of scientific interests of its specialists.

The many problems and methodological procedures in common link aviation and space medicine into a discipline that could be arbitrarily called ecological medicine. This trend is the reason for naming the journal KOSMICHESKAYA

BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA [Space Biology and Aerospace Medicine] in 1978, 10 years after its inception. It should be noted that the American analogue of our periodical underwent a similar evolution of its title, which reflects the changes in its orientation: JOURNAL OF AVIATION MEDICINE, 1930-1959; AEROSPACE MEDICINE, 1959-1974; AVIATION, SPACE AND ENVIRONMENTAL MEDICINE, 1975.

Our journal publishes articles dealing with a wide range of problems of aerospace medicine, biology and psychology. It contains the following rubrics: editorials, surveys, experimental and general theoretical research, clinical studies, brief reports, discussions, letters to the editor, book reviews, current events and information.

The journal is printed in about 1500 copies, about 300 of which are sent to foreign subscribers (in 12 socialist and 15 capitalist countries). In the United States, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA is completely translated into English and published in a small printing. The journal regularly publishes articles by foreign specialists, including results of joint space and laboratory investigations. Many works have been published by scientists from the Polish People's Republic, Czechoslovak Socialist Republic, People's Republic of Bulgaria, Hungarian People's Republic, Republic of Cuba, Socialist Republic of Vietnam, German Democratic Republic, Mongolian People's Republic, French Republic, Republic of India and the United States. A special issue of our journal, like an American one, contained articles by Soviet and American authors.

It should be noted that KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA is in first place amount periodicals published by Meditsina Publishing House, according to share of published works by foreign specialists. This is indicative of the authority of the journal, the desire of authors from other countries to be published in it and, consequently, its noble role in development of scientific collaboration among scientists and specialists of the whole world.

As we know, space biology and medicine, which is based on the theoretical and methodological ideas and help of many biological and medical disciplines (primarily aviation medicine), became efficiently involved in biological exploration of space routes, medical support of spaceflights, development of life-support systems, decisions pertaining to other scientific and practical problems of space exploration. But space biology and medicine did not limit itself to this. Using the unique opportunities offered in connection with investigation of new factors, conditions and approaches, it deepened knowledge about the fundamental bases of biology and medicine, it inriched medicine with valuable observations, criteria and methodological approaches.

To date, space biology and medicine has been definitively formed into an independent discipline which has a theoretical foundation, its own methodological procedures, system of concepts and terminology.

The urgent need to establish a specialized periodical in 1967 was attributable to the rapid development of our field of knowledge and corresponding growth in number of publications. quantitative scientific analysis of materials contained in a retrospective bibiliography [2, 3] revealed that, while a total of 4382

published works were registered in the first 5 years of the manned spaceflight era (1961-1965), they numbered 8082 in the second 5 years (1966-1970), i.e., 184.4% of the initial level. The increment for publications in Russian was 311.2%. True, in the next decade, there was slower increase in number of publications and even a tendency (in the foreign language press) toward a decline.

Also noteworthy is the fact that the share of publications in Russian dealing with space biology and medicine (including psychology) increased from 30 to 50-60% in 20 years (1960-1980), whereas this parameter constituted about 20% for all scientific literature [1, 4].

The link between space biology and aerospace medicine, on the one hand, and numerous allied disciplines, on the other, turned out to be mutually beneficial. At the present time, a wide range of disciplines cooperates in this field. Space biology and aerospace medicine is really part of the life of biomedical, sociopsychological and engineering-technical fields, which is illustrated by the diversity of the scientific specialties reflected in articles published in our journal.

In the last 20 years, there has been a significant increase in number of general theoretical articles dealing with basic scientific problems. For example, while 36 surveys and theoretical works were published in the first decade (1967-1976), there were already 88 in the second (1977-1986), 46 being referable to the last 5 years. In particular, the following philosophical and general biological papers were published: "Man in Space" by O. G. Gazenko (1984), "Philosophical Questions of Adaptation Theory" by B. S. Alyakrinskiy (1986), "Some Philosophical Aspects of the Problem of Man, the Biosphere and Space" by N. A. Agadzhanyan (1979), "Space Biology in Its Third Decade" by O. G. Gazenko and G. P. Parfenov (1982), "Investigations on Biosatellites of the Cosmos Series" by Ye. A. Ilyin (1984).

Spaceflights opened up the opportunity for investigation of such problems of major interest to biology and physiology as gravity biology and gravity physiology, radiobiology, effect of various extreme factors and combinations of such factors. The following surveys were published: "Problem of Accelerations in Aviation Medicine: by P. V. Vasilyev and S. A. Gozulov (1982), "Soviet Research on the Problem of Artificial Gravity: by A. R. Kotovskaya, R. R. Galle and A. A. Shipov (1981), "Electromagnetic Radiofrequency (Microwave) Radiation: Guidelines, Criteria for Setting Standards and "Threshold Dose Levels" by B. I. Davydov (1985), "Constant Low-Frequency Electric and Electromagnetic Fields (Biological Effects, Hygienic Evaluation)" by B. I. Davydov and V. N. Karpov (1982), "Effect of Constant Magnetic Field on the Endocrine System" by G. I. Zagorskaya [1985].

The effects of hypodynamia and hypokinesia investigated by space biology and medicine, the distinctions of fluid-electrolyte metabolism as related to changes in gravity, mechanisms and possibility of adaptation, criteria and range of normal and pathological conditions, including the concept of individual norm, are rather important to physiology and symptomatology ("Orthostatic Instability of Circulation: Role of Deconditioning of Resistive Vessels: by V. M. Khayutin et al., 1984; "Fluid-Electrolyte Homeostasis and Weightlessness" by O. G. Gazenko, A. I. Grigoryev and Yu. V. Natochin, 1980; "Maximum Oxygen Uptake as a Criterion of Human Resistance to Hypoxia, Hyperthermia and Hypothermia" by A. M. Vasilenko (1980).

Of equal interest are problems of biorhythmology, which were also developed thanks to space biology and medicine ("Current Status of Space Biorhythmology" by B. S. Alyakrinskiy, 1977). Investigation of functions and capabilities of the body under working conditions and relevant examination methods with use of radiotelemetry have attracted the attention of specialists in occupational and sports medicine ("Capabilities of Ultrasound Methods in Assessing Hemodynamic Characteristics of the Cardiovascular and Cerebrovascular Systems" by L. G. Simonov and M. S. Felgenbeym, 1986; "Ultrasonic Dopplerography in Flight" by V. S. Bednenko and A. N. Kozlov, 1983).

The problem of developing engineering systems for manned spaceflights raised acute problems of ergonomic qualities of equipment, engineering psychology and medicopsychological aspects of new equipment, which is of deciding significance to most industrial sectors at this stage of the scientific and technological revolution ("Engineering Psychological Guidelines for Optimization of Flight Vehicle Control Systems" by V. A. Bodrov and G. M. Zarakovskiy, 1978).

Problems facing space biology and aerospace medicine made it necessary to pursue in-depth investigation of morphology and functions of the vestibular and other sensory systems of man which, of course, strengthened the theoretical and practical foundation of physiology and medicine. This aspect of fruitful interaction of our field of knowledge with physiology and medicine was also adequately reflected in our journal ("Interlabyrinthine Asymmetry, Vestibular Dysfunction and Space Motion Sickness" by I. I. Bryanov, 1986; "Structure and Function of Otoliths" by A. A. Shipov and A. V. Kondrachuk, 1986; "Human Visual Work Capacity With Exposure to Light at High Levels of Brightness" by V. I. Kartsev, 1981).

Experience in medical and psychological screening, expert certification and training of cosmonauts, dynamic observation of health status, manning crews with consideration of psychological compatibility of crew members, providing for psychological support and development of methods of controlling status and work capacity are drawing the attention of many specialists concerned with screening and training of personnel for different types of work in the national economy. This direction of research, which meets the needs of occupational and social psychology was also reflected on the pages of our journal ("Inception of Soviet System of Professional Screening of Cosmonauts" by M. D. Vyadro and I. I. Bryanov, 1986; "Psychophysiological Screening: Status and Future" by N. N. Gurovskiy and M. I. Novikov, 1981; "Basic Directions and Guidelines for Expert Psychological Certification of Cosmonauts" by K. K. Ioseliani, A. L. Narinskaya and Sh. R. Khisambeyev, 1982; "Prevention of Psychoemotional Disturbances Using Psychological Support Agents During Long-Term Spaceflights" by V. I. Myasnikov and O. P. Kozerenko, 1981; "Psychological Guidelines for Active Recreation During Long-Term Spaceflights" by G. M. Zarakovskiy and S. L. Rysakov, 1972).

The system of assuring flight safety, search and rescue, assistance and survival in cases of accident and under adverse climate and geographic conditions can also be used in many forms of human activity and diverse expeditions ("Stages of Development of the Problem of Flight Safety in Aviation Medicine" by V. A. Ponomarenko, 1986; "Diet During Mountain Ascents" by M. S. Belakovskiy, Ye. B. Gippenreyter and A. S. Ushakov, 1983; "Water Intake During Mountain Ascents" by Ye. B. Gippenreyter, M. S. Belakovskiy and S. V. Chizhov, 1983).

Investigation of semi-self-contained and self-contained life-support systems, depening of our knowledge about the specifications and habitability of confined quarters, including the question of toxicology of new synthetics, as well as many problems of optimizing of working conditions and schedules gave impetus to development of hygienic disciplines having a direct bearing on the most varied sectors of the national economy ("Hygiene and Toxicology of Waste Gases From Human Vital Functions" by V. V. Kustov and A. A. Tiunov, 1980; "Problem of Combined Evaluation of Construction Polymers" by G. I. Solomin, 1985; "Development of Guidelines for Setting Physiological and Hygienic Standards for Noise in Aerospace Medicine" by Yu. V. Krylov, 1984).

The research equipment, methodological procedures and criteria for functional diagnostics, which are being developed in connection with the requirements of space biology and aerospace medicine, meet the pressing needs of medicine and are being used on an increasingly broad scale in practical health care. The creative collaboration and fruitful interaction between aviation and space medicine are presently being manifested on a new, higher level (Space Medicine to Service Science and Health Care" by B. S. Alyakrinskiy, 1982; "Advances in Aviation Medicine to Serve Practice" by P. V. Vasilyev and A. A. Gyurdzhian, 1983; "Cosmonautics and Development of Aviation Medicine" by N. M. Rudnyy and A. A. Gyurdzhian, 1981).

Space biology and aerospace medicine, in close cooperation with such progressive sectors of engineering as aviation and cosmonautcis, made wide use of the advances in computer engineering and mathematical modeling of biological and physiological processes. Publication in this journal of several serious scientific surveys and original research on these matters was instrumental in introduction of these methods in physiology and medicine ("Mathematical Models of Fluid-Electrolyte Metabolism" by A. I. Grigoryev and V. V. Verigo, 1986; "Some Problems Involved in Use of Mathematical Methods for Evaluation of Pathophysiological Changes" by O. G. Gazenko and V. V. Verigo, 1979; "Feasibility of Using Mathematical Models for Analysis of Immunological Phenomena" by V. N. Krutko, 1981; "Current Directions of Biophysical Investigation of Vestibular Function" by A. A. Shipov, 1976).

Thus, it can be considered that space biology and aerospace medicine and its printed scientific organ are making a definite contribution to development of new biomedical thinking with respect to both formulation of a number of fundamental problems and decision of practical and methodological problems of modern medical science.

Apparently, herein lies the basic cause of involvement of a wide range of specialists in space biology and aerospace medicine, and the diversity of fields covered in the journal.

We have already cited above some of the scientific analytic parameters of development of space biology and medicine. Scientific analysis methods can be beneficial to analysis and improvement of the journal's performance. Using the "Science Citation Index"--SCI[6], S. A. Rozhkov and S. G. Kara-Murza [5] drew a comparison of the structure of bibliographic references as one of the indicators of cognitive resources used by authors in KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA and AVIATION, SPACE AND ENVIRONMENTAL MEDICINE. We

believe that this index is only the first step in this direction, and that such work should be continued.

In the summer of 1986, within the framework of the 8th All-Union Conference on Space Biology and Aerospace Medicine, which convened in Kaluga, a conference was held with readers of our journal, and a questionnaire was distributed among them with questions about the means of upgrading the journal. The answers contained in more than 200 questionnaires were analyzed and generalized.

The vast majority of readers who filled out the questionnaire indicated that they were satisfied with the journal, and that it is of substantial help in their research. In essence they approved of its orientation, structure and style. The editorial board paid special attention to critical comments and wishes of readers.

Many readers noted that manuscripts of articles are not processed fast enough in the editorial office, there is too great a dealy in publishing them, and voiced their insistent wish for the journal to be published monthly.

In the questionnaires, there were frequent recommendations to publish more surveys, generalizing and analytical articles, in particular, methodological ones and those referable to data in the foreign press. The readers were not entirely satisfied with the title of the journal; in their opinion, it is cumbersome and does not adequately reflect the topics of published works. There were some criticisms of how articles were written up. It was suggested that each article begin on a new page.

Readers considered it a beneficial practice to give some priority to publication of works by individuals preparing their dissertations and young scientists, as well as articles from outlying regions. Some readers proposed that a special rubric be added for articles recommended by young scientist councils.

In several of the questionnaires, it was suggested that there be more detailed rubrics (permanent or temporary). There were some comments concerning the need for stricter editing of articles with respect to terminology and metrology.

We often encountered the wish to publish more articles on particular aspects (apparently, according to the scientific interests of those polled). But we are inclined to list here some of the wishes: to shed more detailed light on questions of training aviation physicians and specialists; cite more examples from clinical practice; publish works on a broad anthropological and ecological level; hold more frequent debates and discussion of methodological approaches; give more space to current events, reports on congresses, conferences and symposiums, including foreign ones; also to publish more often reports and reviews of Soviet and foreign books and periodicals, international scientific collaboration; publish more articles concerning introduction of the results of space research in health care practice.

There were also some rather contradictory opinions. Some readers consider the journal to be too academic, not adequately linked with practice. Others would like to see more theoretical works and fewer narrowly specialized and practical articles.

Most readers responded in the affirmative to the question of desirability of publishing special topical issues of the journal. However, many of them viewed this as a threat that it would cause even greater delay in publication of articles waiting their turn. For this reason, they propose publication of an additional topical issue.

The suggestion to provide with each article, in addition to an abstract, a brief but meaningful annotation in English merits attention. In this respect, it should be noted that the abstracts submitted to the editorial office that are to be translated into English often fail to be informative enough. The abstract often merely states the issue covered in the article, but does not reflect the purpose of the study, methods, results and main conclusions. An abstract should contain all this information without being substantially longer than the one furnished at the present time.

Since the start of 1987, the editorial board is requesting authors to furnish key words for their articles, which will help systematize, file and retrieve information with use of computers.

The editorial board and editorial council of the journal thanks all readers who voiced their comments and wishes, which will be examined thoroughly, and they also ask that they continue to help in the further improvement of our journal with their advice and suggestions.

Soviet space biology, aviation and space medicine are faced with major and responsible tasks in the remaining years of the 12th Five-Year Plan. The plans for accelerated socioeconomic development of our country, outlined by the Communist Party and Soviet State, are based on progress of science and technology, in which aviation and cosmonautics hold one of the leading places.

The current stage of space exploration, which is characterized by a turn to long-term orbital flights and interplanetary travel in multipassenger spacecraft, requires in-depth analysis of accumulated scientific material, theoretical generalizations and research in new directions in order to preserve the health of crews, assure safety of flights, hygienic and psychological conditions for a full life, efficient and reliable performance of man in the man-spacecraft system.

In addition to the scientific and practical tasks listed above, which are related to progress of aerospace technology, space biology and medicine, we must deepen our knowledge about basic biological and physiological processes, mechanisms and capacities for adaptation to various environmental and working conditions, methods and criteria for assessing man's condition, his individual distinctions, means of enhancing man's resistance, strengthening his health, providing optimum conditions for a full life and successful performance, basic ergonomic problems of human labor in the era of the scientific and technological revolution, psychological and sociopsychological aspects of labor in different sectors of the national economy, regions of earth and conditions of special expeditions, anthropological-ecological problems and many others, which can be reduced to the four following global problems: man and the environment, man and labor, man and modern technology, the human factor in solving problems of acceleration of social and economic development of our country.

The fruitful solution of these problems depends largely on the performance of the journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA.

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SURVEYS

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TRACE-ELEMENT METABOLISM IN MAN AND ANIMALS IN THE PRESENCE OF HYPOXIC STATES OF DIVERSE ETIOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 26 Oct 85) pp 10-16

[Article by V. V. Nasolodin and V. Ya. Rusin]

[English abstract from source] This paper reviews reported data and results obtained by the present authors which describe metabolic pathways of trace elements in humans and animals during hypoxia of different origin, discusses possible causes and symptoms of their deficiency and presents methods of restoring the balance of trace elements.

[Text] At the present time, many researchers are paying attention to the study of metabolism of trace elements in different groups of people, as related to their age, sex, occupation and other factors. The great interest in this problem is attributable to the high biological activity of trace elements and their involvement in a number of vital biochemical processes: redox, tissue respiration, hemopoiesis, organization of immune protection, etc. High biological activity of trace elements is manifested when they are incorporated in the structure of transmitters, hormones, enzymes and vitamins; trace elements are involved in their biosynthesis, enhance and control the activity thereof, as well as corresponding synthetic substitutes.

However, in spite of the exceptionally important role of trace elements, their metabolism in the body under the effect of various extreme factors (in particular hypoxic states) has been studied extremely little. Since adaptation to hypoxia of diverse etiology has much in common with adaptation to intensive muscular activity, it was expedient to generalize here information about the dynamics of trace element levels in blood and organs, not only in the presence of hypoxic states, but muscular strain asssociated with hypoxia.

On the basis of the rather sparse literature, we succeeded in determining that there was increase in activity of metalloenzymes in blood and tissues in the presence of various forms of hypoxia which, in turn, could cause elevation of levels of trace elements, since the latter are either contained in enzymes or are nonspecific activators of enzymes [34, 49, 50]. Such a correlation was observed the most often between levels of iron and copper in tissues, on the one hand, and activity of cytochromoxidase, succinate dehydrogenase, catalase,

ceruloplasmin and others, on the other hand [33, 34]. There is information to the effect that, in the presence of various forms of hypoxia, there is increased saturation of red blood cells with iron, manganese, copper, nickel and vanadium due to redistribution of trace elements in the body [3]. A. M. Mirokilova [23], who studied iron levels in children living at different altitudes in the Pamirs, discovered progressive elevation of iron in blood. The studies of V. D. Savve [44] established that, in the presence of hypoxia, there is significant increase in incorporation of radioactive iron in hemoglobin and bone marrow. In the case of administration of radioactive iron after a 48 h stay in a pressure chamber it was found that its incorporation in hemoglobin was 8-10 times more than at normal atmospheric pressure [44]. During ascent to a high altitude, there was 1.5-2-fold increase in absorption of iron, and the serum iron level had a tendency toward decline. Such a decrease in plasma iron could be attributed to the fact that some of it passes from blood into bone marrow for synthesis of hemoglobin which, in turn, is instrumental in more effective function of organ and tissues during adaptation to high altitude [2, 8]. K. A. Khasanova and I. Ya. Bobodzhayev [51], who studied trace-element levels in residents of high-altitude regions (3600 m altitude), revealed a decline of intracellular iron in blood and elevation of copper and manganese that was correlated with the altitude of the region. The drop of blood iron level, in spite of the hypoxic stimulus, could serve as an indirect indication of its deficiency in the body. Serum iron deficiency (46.7 μg%, versus the normal 100-120 μg%) was found in 53.4% of the tested residents of the Pamirs (altitude 3600-4200 m). Low functional parameters of hemocytoblasts were noted in 17% of the population [5].

In experiments on animals (dogs and rats) with hypoxia induced by bloodletting or stay in pressure chamber, an increase was found in amount and activity of plasma iron referable to ferritin iron. The migration of ferritin into blood plasma was associated with incorporation of its iron into erythrocytes. After acute hemorrhage, incorporation of iron in red cells was twice as fast as in the control [17], while a 2-h stay of animals in a pressure chamber (8000 m altitude) was associated with increase in concentration of copper and iron in the blood, iron in the brain, liver and kidneys [33]. Concurrently with the increase in concentration of trace elements, there was increase in activity of respiratory metaaloenzymes in the brain, myocardium and kidneys. The increase in levels of trace elements in some organs and tissues under hypoxic conditions is perhaps related to the redis-ribution of trace elements, their additional migration from a reservoir and formation of new molecules of enzymes and other metal-protein compounds essential to restore respiration, remove products of impaired metabolism and detoxification of cyanide.

Analogous changes in blood trace element levels were demonstrated in the presence of some pathological states associated with hypoxia. Patients with chronic pneumonia presented an increase in blood plasma and red cell concentration of copper and zinc. The extent of elevation of levels of these trace elements in blood was directly related to the stage and phase of disease, as well as extent of pulmonary and cardiac insufficiency [48]. The increase in amount of copper and zinc in erythrocytes is due to accumulation of these trace elements within each red cell [1].

However, not all forms of hypoxia are accompanied by a rise in level of trace elements in blood. An increase in trace elements was observed as an adaptive

response to hypoxia in the presence of hypoxic hypoxia with signs of marked respiratory acidosis. With this form of hypoxia, there was a 1.5-2-fold increase in trace elements of plasma and formed blood elements. The difference was even greater with a severe extent of hypxoai, probably due to intensification of metabolism of trace elements, increase in permeability of cell membranes under the effect of hypoxia and migration into blood of ions of metals and metalloenzymes [7, 30]. Low levels of trace elements were noted in the presence of hypoxic hypoxia as well as deficiency anemia of alimentary etiology.

Clinical observation of pneumoconiosis patients can serve as another example of the different changes in concentration of trace elements (in particular, iron) in blood with hypoxia. It was established that there was significant increase in blood iron content with grade I respiratory insufficiency. Its level remained high with grade II respiratory insufficiency (however, there was some decrease in content). With marked, grate III respiratory insufficiency, blood iron level was considerably lower than in the two preceding groups [22]. It can be assumed that, at the early stages of respiratory insufficiency, there are still some compensatory reserves, and the rise in iron level is attributable to an adpative response to developing hypoxia. At the late stage of hypoxia, there is depletion of these compensatory reactions due to dramatic decrease in iron supply of the body. The studies of A. P. Yurtseva [52] can serve to confirm this; she observed a negative iron balance in pneumonia cases. In the presence of marked hyperferremia, there was diminished saturation of serum transferrin with iron, dramatic reduction of iron supply in the liver, spleen and bone marrow. Pneumonia patients presented dramatic increase in excretion in urine of manganeses (by a factor of 4.3), iron, copper and titanium (by a factor of 3.5), aluminum and silicon (by a factor of 2.8), as compared to healthy people [48].

It is known that there is intensification of metabolic processes under the effect of exercise, with increased excretion of some organic and inorganic substances; consequently, there is change in levels of the latter in organs and tissues [53, 54].

There are few observations indicative of a relationship between levels of trace elements in blood and nature of muscular exercise, its scope, intensity and conditioning of the body. The studies of some authors established that there was an increase in iron content of formed blood elements, concurrently with growth of muscles and their oxygen requirement, under the influence of regular muscular exercise [24, 36]. Concurrently with increase in concentrations of iron, copper, manganese and zinc in blood cells, there was increase in physical work capacity of athletes [11, 19, 24]. Curiously enough, in the course of adaptation to exercise loads, athletes of junior classes showed accumulation of copper and manganese in formed blood elements at the start of active training. In sports masters, iron, copper and manganese levels in blood cells were higher than in novices [24, 37]. It is a known fact that iron, copper, manganese and zinc ions are not only the catalytic centers of oxidative metalloenzymes, but have oxidative action in a free state [18, 56, 76]. For this reason, accumulation of trace elements in blood cells of athletes and, consequently, increase in oxygen-transport capacity can be viewed as a manifestation of active adaptation to hypoxia during exercise.

Investigations of dynamics of trace element levels in blood and organs under the influence of single occurrence of physical strain are of special interest. It is important to stress that exercise loads differing in nature and duration elicited far from similar changes in concentration of trace elements in blood. Exercise on a cycle ergometer of even moderate intensity elicited reliable elevation of plasma copper and manganese levels of unconditioned individuals [55]. E. Presiler and R. Kabsa [74] observed noticeable increase in plasma iron concentration in swimmers and oarsmen. Longer exercise (5000 m cross-country run) was associated with noticeable decrease in blood iron content with relative stability of copper and manganese levels [19].

Our special observations of athletes in competitions revealed that a 1500-m race was associated with noticeable elevation of iron, copper and manganese levels in plasma and formed blood elements. Diametrically opposite changes were observed in trace element content of different fractions of blood under the influence of 3000-m races and 5-km ski races. While iron, copper and manganese levels dropped appreciably in plasma, they rose significantly in formed blood elements. When contests were extended to 3 h (50-km ski race), there was a decrease in concentration of trace elements in both blood fractions [26, 38, 40].

Nor is there any question that the dynamics of trace element levels in different systems of the body depend on many factors, including activity of the adrenosympathetic system [4, 20]. It is also known that, provided it is intense and long enough, physical exercise usually enhances adrenosympathetic activity, which is characterized by an undulant pattern [9, 21, 31, 32]. The increase in excretion in blood of catecholamines to assure efficient function of biological systems under extreme conditions and creation of a larger supply of trace elements in blood by mobilizing their reserves to enhance redox processes can be the explanation for increase in blood iron, copper and manganese levels under the effect of brief but intensive exercise, on the basis of the relationship between trace elements and the adrenosympathetic system. In the case of longer (up to 20 min) and rather intense exercise, adaptation to working hypoxia may be associated with build-up of acidosis, impairment of cell membrane permeability, decrease in concentration of trace elements in plasma with concurrent accumulation of their ions in blood cells. This compensatory reaction indicates, as it does with other forms of hypoxia, intensification of redox processes in the body. Dramatic decrease in trace elements of both fractions of blood with even longer exercise (up to 3 h) is apparently attributable not only to depression of the adrenosympathetic system, but decrease in readily mobile spare supply of trace elements [35]. The latter was confirmed in special balance studies on athletes on days of competitions involving distances of 15, 30 and 50 km, when a dramatically negative 24-h balance of iron, copper, manganese and zinc was observed [25, 27, 39].

Some rather curious results were obtained from model experiments on dogs. A tendency toward rise of levels of iron, copper and silicon in canine blood was observed, along with increased work capacity, under the effect of moderate systematic dynamic loads for 6 weeks. Significant increase in exercise loads was associated with incipient decline in concentration of hemoglobin in blood, erythrocyte count and trace element, particularly plasma iron [12]. Use of heavy physical loads to the point of fatigue twice a day caused a decrease in the animals' concentration of iron, copper and zinc in plasma and formed

blood elements. Concurrently, there was a decline of trace element levels in most internal organs, which is indicative of drastic depletion of trace elements in the body [12, 43].

Impairment of balance of trace elements as a result of their increased use or inadequate intake with food is usually associated with dramatic change in body functions. It is known, for example, that inadequate intake of iron is instrumental in development of iron-deficient anemia and manifestation of such symptoms as weakness, irritability, diminished immunoresistance and physical work capacity, longer recovery time for the latter after an exercise load [6, 10, 13, 14, 16, 35, 58, 62, 72, 75]. The more severe the iron deficiency, the more noticeable is the decline of its level in serum and saturation in transferrin, the more marked the decrease in concentration of blood hemoglobin, number of sideroblasts, amount of ferritin and iron in bone marrow, the more significant the decrease in activity of iron-containing enzymes--catalase, peroxidase, succinate dehydrogenase, cytochromoxidase and others. Concurrently, there is elevation of levels of erythrocytic protoporphyrin and haptoglobin in serum, increase in iron-binding capacity of serum and absorption of iron in the intestine, with impairment of proportion of other trace elements in organs and tissues [10, 60].

When there is a dietary copper deficiency, there is decrease in activity of ferroxidase, concentration of iron and hemoglobin in blood; life span of red cells is reduced and their maturation is retarded [73]. Decrease in copper concentration in blood, diminished supply in organs, reduced activity of copper-containing oxidases, including ceruloplasmin, are the chief signs of copper deficiency [45, 46, 57, 61, 65, 67]. In the case of a severe copper deficiency, neutropenia and hypochromic anemia, retarded growth, vascular disorders, depigmentation of the skin and hair, abnormal bone formation, myocardial fibrosis and other clinical manfiestations are observed [57, 59, 65, 69-71].

A manganese deficiency may also be associated with many structural and physiological defects. The observed typical symptoms depended on the diet and its manganese content. In animals, the symptoms were diminished height, defective bones, impaired hemopoiesis, fat metabolism and reproduction, congenital ataxia and structural changes in various cellular organelles [66, 68, 70]. In man, nausea and vomiting, rapid weight loss and changes in hair color were observed in the case of a manganese-deficient diet [57].

Retarded growth and sexual maturation, diminished concentration of zinc in plasma, red blood cells, urine and hair may be signs of a zinc deficiency. It can be associated with parakeratotic skin lesions, alopecia and anorexia, loss of taste and olfaction [63, 68, 70]. A zinc deficiency is sometimes associated with an iron deficiency, which may be manifested by severe iron-deficient anemia, in addition to the above-mentioned symptoms [47]. A zinc deficiency may occur in the case of parenteral feeding, chronic febrile infectious diseases, cirrhosis of the liver, alcoholism or kidney diseases.

Of the numerous factors instrumental in development of trace element deficiency, an unbalanced proportion of trace elements and other elements of the diet should be singled out in particular; in a number of instances these leads to a deficiency in the body, attenuation of synthesis of biologically active

compounds affecting and altering functions of many vital systems. Unilateral preference for some foods, significant loss of trace elements in cooking, freezing and prolonged storage of foods, as well as prolonged stress situations, may play a part among interrelated causes of inadequate supply of trace elements.

In view of the fact that there is significant increase in rate of utilization of trace elements for synthesis of metal-protein compounds in the presence of hypoxia, which in turn leads to reduction of trace-element supply with all the ensuing consequences, special attention should be given to providing the body with trace elements. There is information to the effect that, after administration of iron, copper and cobalt to intact animals there was noticeable increase in nonheme and hemin iron, copper in mitochondria of the brain, liver, and in activity of the succinate dehydrogenase system in tissues [34]. L. M. Guseynova et al. [15] established that copper, cobalt, iron, manganese and other metals in specific doses visibly improved adaptation to hypoxia. The mechanism of action of these trace elements is quite complicated. It consists, first of all, of intensifying external respiration, increasing activity of many oxidative metalloenzymes, stimulating effect on blood-forming organs, hemopoiesis and other functions.

Our chronic experiments on animals and observations of various groups of essentially healthy people revealed that supplementing the diet with trace elements in conjunction with other biologically substances had a beneficial effect on biological functions: there was increase in amount of trace elements in blood and internal organs, hemoglobin and erythrocyte count, activity of peroxidase and ceruloplasmin, improvement of the body's defenses and physical work capacity [28, 29, 38-42].

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PHYSIOLOGICAL AND BIOCHEMICAL ASPECTS OF TOXIC EFFECTS OF OXIDANTS IN MAN'S ENVIRONMENT (AIR, WATER)

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[Article by Z. P. Pak and G. V. Lobacheva]

[English abstract from source] This paper gives a review of published data about physiological and biochemical aspects of the toxic effect of oxygen, ozone, hydrogen peroxide, nitrogen oxide and haloid-containing disinfectants on the human body. The mechanism of action of various oxidants in terms of free radical reactions is analyzed. The oxidant sensitivity of membrane structures, sulfhydryl compounds, proteins, enzymes and the genetic apparatus of the cell is evaluated. The effect of oxidants on the function and structure of erythrocytes, red marrow, blood coagulation, immunity, histological and histochemical structure of organs and tissues is described.

[Text] As the area of use of chemicals containing oxidants in different sectors of the national economy and everyday life broadens, they become a permanent component of man's environment and a source of environmental pollution. Oxidants are also finding practical application in life-support systems of confined quarters used for different purposes [10, 43, 46]. The toxicity of oxygen is one of the limiting factors in establishing its optimum level and partial pressure in the artificial gas atmosphere of manned compartments [43]. Investigation of the mechanisms of toxic effect of oxidants on biological systems is important to prevention of potential poisoning and development of methods of protection against their deleterious effect.

There are surveys in the scientific literature that deal with the mechanism of toxic action of different substances with a high oxidative potential: oxygen [9, 20, 23, 71], ozone [99], hydrogen peroxide [26, 47], iodine [32], chlorine [14], nitric acid and nitrogen oxides [13]. A comparative analysis has been made of the free-radical action of oxygen, ozone and radiation [82]. However, there are no generalizing works dealing with the toxic effects of various oxidants on animals and man.

Stimulation of free-radical processes is the chief factor in the mechanism of action of oxidants [9, 20, 23, 26, 82, 92]. The free-radical theory is

applicable not only to oxygen-containing oxidants, but to halogens. For example, Henderson and Haggard [14] believed that the essence of the effect of chlorine on a living system consists of the fact that, by affecting tissues, it removes their hydrogen, forming hydrochloric acid and releasing atomic oxygen, which acts at the time it is released.

Free-radical reactions cause interaction between oxidants and most biochemical components of the cell, and they cause degradation of vital molecules [12, 65, 92]. In this respect, much importance is attributed to the superoxide radical ($O_2^{\cdot}$), which appears as a result of a wide spectrum of biochemical reactions, including autooxidation of thiols and oxyhemoglobin, "leakage" of electrons in mitochondrial chains of electron transfer, impaired odygen metabolism of oxygen, as well as under the effect of exposure of cellular systems to biologically active compounds. Superoxide dismutase is the protective enzyme against the O_2^{-}. radical it catalyzes the reaction: $O_2^{-}. + O_2^{-}. + 2H^+ \rightarrow H_2O_2 + O_2$ [5, 64, 73, 77]. It was established that superoxide dismutase can also inhibit production of singlet oxygen ($^1O_2$) [108]. The increase in superoxide dismutase activity in response to oxidants [19, 25, 77] is indicative of triggering of defense mechanisms. The observed decline in activity of the enzyme [73] is apparently related to exceeding the defense capacities with respect to the O_2^{-} radical.

Hydrogen peroxide (H_2O_2) is one of the intermediate products of reactions involving oxdants; it is extremely reactive, rather stable and can accumulate in aqueous media. Catalase and peroxidase serve as protection against the toxic effect of hydrogen peroxide [61, 86]. Both an increase in catalase activity, related to the body's defense reaction [98], and its decline have been observed, as a result of impairment of redox processes and accumulation of incompletely oxidized metabolic products [4, 40] and direct inactivation by hydrogen peroxide, to the effect of which it is extremely sensitive [107].

The superoxide radical, which reacts with hydrogen peroxide, leads to formation of a hydroxyl radical (OH.), one of the most reactive free radicals: $O_2^{-}. + H_2O_2 \rightarrow OH^- + OH\cdot + O_2\cdot$. It is formed only after accumulation of a significant amount of H_2O_2, and its production is inhibited by both superoxide dismutase and catalase [64].

Lipid peroxidation is important to the mechanism of toxic action of oxidants. Free radicals affect unsaturated fatty acids with formation of lipid free radicals ($L\cdot$) which, in the presence of oxygen, are readily converted to lipid perioxide radicals ($LO_2.$). The latter are highly reative agents, which elicit a chain of reactions when interacting with adjacent molecules in membrane structures. This process, which is known as auto-oxidation, plays a leading role in membrane injury [12, 36, 61, 68, 94]. Many researchers have mentioned oxidation of membrane lipids of erythrocytes, mitochondria, microsomes, lysosomes and other cell organelles in the presence of oxidants [15, 28-30, 53, 62, 75, 100]. Alpha-tocopherol or vitamin E serves primarily as defense against the cytotoxic effect of lipid peroxides [61, 92, 102].

Of the many compounds that are affected by oxidants, the most attention has been given to thiols [29, 32, 56, 71, 99], which may play the leading role in events on a molecular level, leading to injury to the most important structures. N. Haugaard [71] mentions the involvement of both nonprotein and protein SH groups in interaction with toxic substances that have oxidative properties. Among the

nonprotein sulfhydryl compounds, we can mention reduced glutathione, coenzyme of lipoic acid, coenzyme A and others. These substances, like other sulfhydryl compounds, are oxidized with production of disulfides. D. B. Menzel [83] reported irreversible changes in SH groups under the influence of ozone, which could not be reduced by reductase present in cells, which is indicative in his opinion of deeper oxidation of sulfhydryl than disulfide.

The total amount of proteins and proportion of different fractions, their physicochemical properties (viscosity, solubility), molecular structure and number of functional groups change under the effect of oxidants. There is breakdown of biological complexes. There is change in amino acid composition and in amounts of protein-bound urea and nucleotides [49, 57, 90, 95, 105]. Among the amino acids, the most sensitive ones are histidine, methionine, serine, proline, arginine and tyrosine [57, 95]. D. E. Boehm et al. [52] report that inhibition of amino acid synthesis leads, in addition to impairment of protein synthesis, to loss of cell's capacity to synthesize nicotinic acid, NAD, NADP, folic acid, pantothenic acid and coenzyme A.

Z. S. Gershenovich [16] assumes that there are two molecular mechanisms in the toxicity of oxygen: direct--action on auto-oxidized substances, and indirect--enhancement of primary effect through modification of protein properties. H. E. Stockinger [99] believes that injury to proteins under the effect of ozone is the result of oxidation of SH groups, and the toxic effect is enhanced by the action of free radicals that appear from interaction of the oxidant with SH groups. Change in activity of many enzymes is an important consequence of conformational disturbances in proteins.

It was found that ocidants and products of free-radical oxidation are potent inhibitors of enzymes, and sulfhydryl enzymes are the first to be stricken [9, 26, 32, 109]. Many oxidation-sensitive enzymes and coenzymes were found in the tricarboxylic acid cycle and glycolysis (succinate dehydrogenase, lactate dehydrogenase, malate dehydrogenase, cytochromoxidase, NAD·H, cytochrome *c* reductase, glyceraldehyde-3-phosphate dehydrogenase, pyruvate kinase, phosphofructokinase [33, 53, 56, 83, 87]. C. K. Chow and A. L. Tappel [55] report an increase in activity of two key enzymes of the pentose-phosphate pathway (glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase) under the effect of ozone. Stimulation of the pentose-phosphate pathway was also observed under the effect of oxygen [18, 23, 69]. From the standpoint of active involvement of coenzyme A in sulfhydryl enzymes in fatty acid metabolism, it could be expected that some stages of lipid metabolism may be sensitive to oxidants [71].

Ye. A. Mukhin et al. [33] observed increase in activity of glutamic-oxaloacetic and glutamic-pyruvic transaminases with oxygen poisoning. There are reports of depression of activity of red cell acetylcholinesterase and serum cholinesterase activity by oxidants [48, 50, 67, 88]. A decrease in activity of aspartate and alanine aminotransferases was noted under the effect of nitrogen dioxide [78], while an increase in their activity was reported under the effect of residual amounts of ozone in drinking water [42]. V. Z. Lankin et al. [25] demonstrated both decrease in glutathione lipoperoxidase activity in rat blood and liver in the presence of hyperoxia, and increase in activity of this

enzyme at higher concentrations of oxygen, which the authors relate to its induction of lipid peroxides intensively formed under such conditions.

The diverse enzymes and related metabolic processes subject to the effect of oxidants largely determine the polymorphism of manifestatins of toxic effect of oxidants on the body as a whole and its different systems.

It was shown that haloid-containing disinfectants, hydroperoxide and oxygen at high pressure cause disturbances in oxidative metabolism by depressing enzymes of the respiratory chain and dissociating oxidation from phosphorylation, which leads to less production of energy-rich phosphate bonds. Diminished synthesis of ATP leads, in turn, to injury to other physiologically important systems [7, 17, 28, 44, 101].

Oxidant-caused injury to sensitive cellular structures is also the cause of subsequent functional changes on the cellular and tissular levels. It was established that lipid peroxidation of the mitochondrial membrane leads to its swelling and loss of capacity for oxidative phosphorylation [89, 103]. When lysosome membranes are injured, there is release of acid hydrolases which destroy tissue elements and significantly augment damage [30, 102].

The following mechanisms are distinguished in the toxic effect of oxidants on functional and structural integrity of erythrocytes:

> Formation of lipid peroxides in cell membranes, as a result of which there is damage to the membrane, impairment of its permeability and hemolysis of red blood cells [27, 58, 100]
>
> Decrease in reduction activity in erythrocytes, leading to degradation of hemoglobin, increased production of methemoglobin and carboxyhemoglobin [66, 86]
>
> Loss of activity of enzymes contained in erythrocytes due to direct oxidation (particularly of sulfhydryl groups) and decrease in amount of reducing agents [52, 67, 75, 91]

Migration into blood of products of erythrocyte breakdown leads to stimulation of erythropoiesis in red bone marrow, increase in reticulocyte content of the blood stream and, consequently, increased erythrocyte resistance to hemolysis [8]. A. G. Zhironkin [20] reports on the direct effect of high concentrations of oxygen on the hemopoietic system, which consists of hyperplasia of red bone marrow with activation of erythroblast proliferation, decrease in number of erythrocytes and hemoglobin in blood. Ye. F. Morshchakova et al. [31] have shown that diminished erythropoiesis in the presence of hyperoxia occurs due to decrease in amount of plasma erythropoietin. It is assumed that nitrogen dioxide stimulates renewal of the pool of erythrocytes [87].

The effect of oxidants leads to impairment of blood-clotting processes. R. M. Senior et al. [97] observed accelerated catabolism of fibrinogen and appearance of products of its degradation, increased concentration of blood factor V in the presence of hyperoxia. There are reports of accelerated coagulation of blood and diminished fibrinolytic activity under the effect of chlorine [1] and nitrogen oxides [11].

In concentrations of hundredths of a micromole, hydrogen peroxid changes the form and reaction of platelet release regulated by ADP and thrombin. With micromolar concentrations of H_2O_2, there is inhibition of release of thrombocytic ATP and ADP [54, 93, 101]. In the presence of hyperoxia there is impaired deposition of serotonin in thrombocytes [79]. The change in functions of these cells can affect processes of hemostasis and thrombus formation. R. T. Canoso et al. [54] and R. Rodvien et al. [93] believe that substances that elicit production of peroxide products can prevent thrombus formation by changing aggregation or disaggregation of platelets.

The effects of oxidants also extent to the immune system. There is information indicative of depression of phagocytic activity of neutrophils under the effect of iodine [34] and nitrogen oxides [13]. N. A. Agadzhanyan et al. [2] observed depression of antibody production in the presence of hyperoxia, which was demonstrable both by the antibody titer in peripheral blood and decrease in number of antibody-forming cells in the spleen. According to the data of Y. Matsumura [80], ozone, nitrogen dioxide and sulfur dioxide intensify allergic reactions of guinea pigs to antigen aerosol.

A. Savino et al. [96] report on the effect of ozone on human clelular and humoral immunity. The authors attribute depression of rosette formation by T- and B-lymphocytes to injury to leukocyte membranes caused by free radicals and formed metabolic products, as well as corresponding change in structure of receptors on T- and B-lymphocytes. R. P. Hillam et al. [72] obtained dose-dependent stimulation of cellular immunity under the effect of nitrogen dioxide.

There is information about the nature of changes in histological and histochemical structure of internal organs caused by oxidants [3, 6, 22, 31, 35, 39, 51, 106]. Swelling of the mucosa, plethora and edema of the submucosal layer, hemorrhages, necrosis and necrobiosis of glandular tubules were observed in the stomach under the effect of perchloric acid (ClO_4^- ion). Circulatory disorders were also noted in other organs [51]. With oxygen poisoning, there was dramatic dilatation of vessels and areas of effusion of blood in the heart, liver and kidneys [22]. Glomerulonephritis [3], dystrophic changes in convoluted tubule epithelium [6, 22], endothelium of capillaries of vascular glomerules manifested by appearance of numerous microvilli and swelling of cellular cytoplasm [106], diminished synthesis of high-polymer RNA [31] were observed in the kidneys under the effect of oxidants. In the liver, there was fine and large-droplet fatty dystrophy of hepatocytes [3, 39], lymphoid infiltration of the stroma [35], decompensation of some hepatic lobes with vacular dystrophy of cells [22], increased activity of tissular proteases [49], increase and subsequent decrease in activity of oxidative enzymes NAD and NADP, increase in RNA content, protein and ribisomes [106]. The spleen showed hyperplasia of follicles [3], increase in number of juvenile forms of the lymphoid and myeloid class [35], increase in amount of iron-contianing hemosiderin pigment, which is indicative of increased breakdown of erythrocytes [35, 106]. Edema of capillaries and impairment of their lipid composition were noted in the adrenals [106]. J. L. Vincent and G. A. Lartigau [106] report on the absence of appreciable changes in the pancreas and central nervous system under the effect of a potent oxidant such as ozone. At the same time, Z. A. Aliyeva et al. [6] succeeded in finding vascular plethora and stasis in the brain under the effect of iodine. A. A. Krichevskaya et al. [23] reported changes in protein composition of the brain in the presence of hyperoxia.

Oxidants and products of their transformation have an adverse effect on the genetic system of the cell. Peroxide radicals and hydroperoxide cause arrest of genome replication and cell division [37], inactivation of biologically active replicating DNA [104], break in the double helix of the DNA molecule [74] and injury to polynucleotides [85]. After exposure to ozone, chromosomal breaks were found in a culture of human tissues [63], chromosomal aberrations in human [84] and Chinese hamster lymphocytes [111], as well as inhibition of mitotic activity in cell cultures [76]. At the same time, no mutagenic effect was demonstrated in a study of haloid-containing disinfectants [41], oxygen in high concentrations [110], ozone in doses exceeding the maximum permissible concentration [81].

There can be gerontological consequences from the effect of oxidants [12, 19, 61] since, according to the theory of D. Harman [70], the irreversible damage to components of cells and connective tissues caused by free radicals appearing in the oxidation process are the cause of their aging.

Thus, the mechanism of toxic effect of oxidants is based on free-radical processes, which lead to involvement of membrane structures of the cell, damage to thiol compounds, protein structures and inactivation of enzymes. The effect of oxidants is manifested by injury to formed blood elements, impairment of blood clotting, change in immune reactivity and histochemical structure of organs and tissues, damage to the genetic system of the cell. Free radicals formed during oxidation are responsible for accelerating aging processes.

The polytropic effect of oxidants on living systems is largely attributable to their high antimicrobial properties, thanks to which they are used extensively as decontaminants and preservatives.

The diversity of molecular and cellular structures of the body that are sensitive to the action of oxidants deter ines the broad spectrum of substances, both natural and synthetic, that have antioxidant properties: ascorbic acid, sulfhydryl compounds (cysteine, glutathione), tocopherols (mainly α-tocopherol), ubiquinones, some steroid hormones, polyamines (spermidine, spermine), thiourea, arginine, γ-guanidinobutyric acid, GABA, EDTA, lecithin, selenium, hydroquinone, ionol, naphthols, "etiron," aminasine, caffeine, sodium bromide and others [5, 12, 21, 22, 24, 38, 45, 58-60]. In addition to positive experience with the use of these compounds as detoxifying agents, the mechanism of antioxidant action of a number of substances (phospholipids, some antibiotics) has not yet been definitively determined [12], due to the fact that the mechanisms of toxic action of oxidants have not been sufficiently studied. Consequently, the problem of toxicology of oxidants remains as a pressing one. Its solution would permit a purposeful search for substances with protective anti-oxidant properties.

The possibility of presence of oxidants with high bilogical activity in man's environment requires elaboration of methods of monitoring them in air, water and foods. Considering the difficulty of chemical identification of trace amounts of oxidants and secondary products of oxidation, biological testing of possibly contaminated objects should be considered the most reliable, with use of a broad spectrum of specific physiological and biochemical tests that permit detection of the toxic effect. Development of protection should include

both refinement of methods of purifying air and water to remove deleterious impurities with use of reducing agents, and use of combined agents with a broad spectrum of anti-oxidant action.

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SOME ASPECTS OF SOCIOPSYCHOLOGICAL SCREENING OF FLYING SCHOOL APPLICANTS

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[Article by V. I. Yevdokimov and P. P. Parkhomenko]

[English abstract from source] One hundred and fifty-nine applicants who passed entrance examinations and were admitted to the flight school were kept under careful psychological observation and follow-up. It was found that those applicants who grew and developed in unfavorable conditions, i.e. under the influence of risk factors which include young age to start smoking, nervous shocks in childhood and adolescence, unstable family relations, alcoholic parents, etc., failed and were expelled from the school due to different reasons in a greater number of cases ($p<0.01$). Thus professional selection should include accentuated attention to risk factors that accompanied the years of personality formation which may help predict their inadequacies in psychic adaptation to the flying profession.

[Text] In view of the more complicated conditions and nature of pilot work, there is an increase in requirements of applicants to flying schools, of their sociopsychological qualities [1, 3].

Some domestic problems and means of identifying sociopsychological circumstances of personality formation of applicants were investigated. As applied to screening, domestic problems interested us in the aspect of the personality approach: under what conditions did the applicant's personality form and develop [6-8].

Methods

A total of 159 applicants to a flying school, who had appeared before the expert medical commission for flight certification, passed their entrance examinations and demonstrated a rather high level of development of the main occupationally important mental traits and were enrolled in the first year of flying school were submitted to a comprehensive psychological examination. In addition to tests involving use of forms and equipment used in traditional psychophysiological screening, the examination included some personality-oriented tests: 1) 16 personality factor questionnaire (PFQ), form A, of

R. Cattell; 2) questionnaire to examine typological personality traits (TPT) consisting of 176 questions, 50 of which to test extraversion, 50 for neurotic elements, 50 for asthenic traits and 26 for occupational orientation and physical condition [9]; 3) projective aviation test (PAT), which consisted of 10 aviation-oriented picutres. The subjects were to write a story about the pictures, with mandatory answers to the following questions: "What preceded the illustrated situation? What does the picture show? Who are these people? What is the outcome of the situation?" The conception of story as a model of activity was used as a very general system in interpreting the PAT stories [5].

In addition to these tests, the applicants were presented with a background questionnaire consisting of 60 questions, the answers to which reflected distinctions referable to personality development in childhood and youth, parents' relationship, their attitude toward alcoholic beverages, age at which they began smoking and drinking, social orientation, etc.

Their educational and occupational characteristics were examined in greater detail, and on their basis tentative evaluations were made characterizing the subjects' motivation. Much attention was given to negative, even insignificantly marked traits. In this case, as the personal files were delivered to the receiving commision these circumstances were defined through correspondence with the institution that issued the information. In a final talk for occupational screening, the results of preceding medical and psychological examination of applicants were ascertained, determination was made of the source and nature of motivation, general development.

Results and Discussion

The results of the screening revealed that, already in the course of an attentive examination of the applicants' personal files, it is possible to extract valuable information about the structure of motivation and some individual psychological personality distinctions: gregariousness, industriousness, discipline, extent of development of leadership traits, etc.

Experience in working at a flying school shows that negative personality traits reflected by the characteristics usually coincide entirely with the actual manifestation of students' behavioral reactions. Moreover, the predicted evaluation of learning achievement made solely on the basis of studying personal files (theoretical achievement, educational and occupational characteristics, structure of writing application for enrolment at the school) had a significant correlation in our study ($r = 0.17$; $p<0.05$) to indicators of flying school achievement.

The answers to the background questionnaire were of special significance. For example, the mean age at which they started smoking was in the range of 16-17 years; they first tasted alcholic beverages at 15-16 years. In the last 12 months, 3.8% of the applicants (6 people) had consumed alcohol several times per month, 45.3% several times per year and 50.9% consumed none at all. These data agree in essence with the results of other studies [2]. There were adverse consequences of drinking (conflict situations at work, in school, at home, getting into accidents, etc.) in 10.7% (17 people), including several such instances in 1.9% (3 people).

If we consider that the average age of the applicants is 17-18 years and that there is intense and extreme work ahead of them, such a situation should be considered unsatisfactory, and it requires formation of teetotalling traditions among flying school cadets in the light of the decree of the CPSU Central Commission, "Steps to Oversome Drunkenness and Alcoholism" dated 16 May 1985.

A relatively large number of flying school entrants were from "unhappy" families. In our study, the parents of 18.9% (30 people) of the applicants were separated and 10.7% of the applicants (17 people) characterized the relations between their parents as poor.

Comprehensive pedagogic observation was instituted for 1 year for the applicants who became cadets, and extensive information was gathered, which reflected their achievement in flight, simulator and theoretical training, discipline, social activity, health status, etc.

It should be noted that some degree of difficulties was found in the flight training of most individuals with obviously unfavorable circumstances of personality formation. We found that the average grade for flight achievement was 4.7 (on a 9-point scale) for those with broken families. In cadets whose screening failed to reveal risk factors for personality formation (standard [normative] group) the score was 5.3. Poorest achievement was found in cadets who grew up to families that were at the breakdown stage, and those whose parents drank too much. The average achievement score for this group was 4.1. It is expressly among this group that the largest number was dismissed due to professional unfitness, discipline, physical condition. The number of dismissals from this group constituted 47.1%, which is more than twice the percentage dismissed from the standard group ($p<0.01$).

Correlation and factor analysis of the results of medical and psychological examination as related to achievement at the flying school was used for deeper investigation of the obtained data.* We found that there was minimal correlation between these tags. And this is understandable, since the results obtained from the medical and psychological exmaination affect indirectly the achievement in flight training.

In a number of instances (for example, in the answers in the background questionnaire), the farther in the past they went, the more frank and truthful was their information about themselves. Therein may lie the advantage of the information gained since, in the opinion of a number of scientists [1, 4], ethical elements of personality are conceived at the early stages in life and remain virtually constant for the duration of an individual's life in their main features.

In the course of the examination, it was established that there was a negative correlation between age at which the applicants started smoking and flight

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achievement (r = -0.16; $p<0.05$), general professional screening rating (r = -0.17; $p<0.05$), simulator training (r = -0.17; $p<0.05$) and discipline (r = -0.16; $p<0.05$). Positive correlations were found when we compared the age at which smoking was started and age of alcohol consumption (r = 0.27; $p<0.001$) and frequency of drinking among parents (r = 0.17; $p<0.05$).

It should be noted that, in accordance with established tradition, it is easier for an applicant to be truthful in answering the question of age when he began to smoke than the age at which he started to drink, let alone the frequency of alcohol intake by parents and nature of family relations. For this reason, the age at which smoking was started is indeed an indicator of unfavorable circumstances of personality formation that could have an adverse effect on the process of flight training.

We also found positive correlations between psychological trauma experienced by applicants at a young age and anxiety according to the PAT (r = 0.18; $p<0.05$), asthenia according to the TPT (r = 0.24; $p<0.01$) and incidence of drinking mothers (r = 0.25; $p<0.01$). It should be noted that the applicants interpreted the concept of "trauma in youth" as referring to very dramatic events. As a rule, they reflected actualization by an anxious personality of ordinary situations.

Thus, the mention of mental trauma in youth could characterize, on the one hand, asthenic tendencies in the subjects and, on the other hand, adverse conditions of personality formation.

Factor analysis of the screening results revealed three basic factors. The first factor, which we called general development factor, included with a high positive weight, evaluation of theoretical achievement, average score for certificate and entrance examinations. In this factor, the weights on the extroversion scale in the TPT questionnaire, cyclothymia and intelligence in the PFQ and general sthenia in the PAT were close to significant.

The second factor, which grouped the ratings of professional screening and practical flight training, showed significant weight of some screening tests, general psychological stability according to pedagogic ratings obtained in the course of special physical training. In this factor, the weight of ratings of simulator training and weight of age at which smoking was started were close to being statistically reliable, with opposite sign.

The third factor characterizing conditions of personality formation contained the positive weight of neurotization and asthenia in the TPT. It also contained the positive weight of answers to most questions in the background questionnaire characterizing the applicants' parents' attitude toward drinking, frequency of alcohol intake, adverse consequences of drinking in the family, trauma in youth, etc.

Individual analysis of the PAT stories revealed that, in a number of cases, the psychodiagnostic information revealed significant emotoinal experiences of the subjects, nature of family relations; it predicted the applicant's attitude toward discipline and alcoholic beverages which could also serve, to some extent, as "risk factor" indicators. These characteristics were

probabilistic, but they permitted forecasting the subjects' behavior, which was subsequently defined in the course of talks and further observation.

As a result of this study, it can also be concluded that laying emphasis on sociopsychological aspects of personality formation of a future pilot enables us to predict inadequate means of psychological adaptation to extreme conditions of professional work, which are manifested by asthenic tendencies and a tendency toward nonconformist behavior.

Starting to smoke at an early age (15 years or younger), existence of mental trauma in youth, frequent alcohol intake by parents (at least once a month) and unstable family relations can be considered risk factors indicative of adverse conditions of personality formation in the standardized talk (questionnaire) with the applicant.

The extreme nature of flying work which imposes greater demands of the nervous and psychological system of flight personnel requires formation of teetotalling mind sets in flying school cadets in the light of the decree of the CPSU Central Committee, "Measures to Overcome Drunkenness and Alcoholism."

Thus, the time is ripe for deeper investigation of sociopsychological traits of applicants for operator professions and broader use of the methods of social psychodiagnosis in the armamentarium of professional screening.

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CARDIAC CONTRACTILITY IN WEIGHTLESSNESS ACCORDING TO SPATIAL BALLISTOCARDIOGRAPHY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 28 Feb 86) pp 26-31

[Article by R. M. Bayevskiy, P. S. Chattarjee, I. I. Funtova and M. D. Zakatov (USSR and Republic of India)]

[English abstract from source] In the joint Soviet-Indian space flight the method of spatial ballistocardiography was used to investigate the cardiac function in flight. The piezoelectric transducer was placed between the scapulae and its orientation was varied relative to the three axes of the body. Measurements were taken twice before, twice during and twice after flight. Ballistocardiograms were analyzed in terms of their amplitude, time and spectral parameters. It was found that in microgravity the energy of cardiac contractions developed spatial redistribution. It was also demonstrated that the cardiovascular function showed individual variability.

[Text] As we know, body fluids are redistributed in microcravity, and they are shifted to the upper part of th body, which leads to increased blood in the pulmonary vascular system and redistribution of load to the right and left heart. Ballistocardiography may be important to evaluation of cardiac contractility under such conditions. Ballistocardiograms (BCG) previously taken during spaceflights made it possible to demonstrate a link between strength and coordination of cardiac contractions, on the one hand, and duration of spaceflight, intensity of exercise, as well as specific distinctions of the acute period of adaptation to weightlessness, on the other [3-5]. However, in these studies, the BCG was recorded by the traditional method only in the direction of the body's long axis (head-legs axis), which did not permit evaluation of redistribution of mechanical energy of contractions due to changes in position of the heart in the chest and shift of blood to the upper half of the body. To solve this problem, spatial ballistocardiography may be an adequate method; here, body movements related to cardiac function are recorded in three mutually perpendicular directions. The first results of using this method to study cardiac contractility in experiments with antiorthostatic [head-down tilt] hypokinesia [7] and during an actual spaceflight [8] have been published.

We submit here some of the results of using spatial ballistocardiography to examine the circulatory system of crew members during the joint Soviet-Indian spaceflight.

The method of spatial ballistocardiography was used for the first time during this mission, and it enabled us to examine more fully the mechanical activity of the heart at the first stage of human adaptation to weightlessness.

Methods

A BCG-1 (PAM) transducer, developed and manufactured at the Gorkiy Institute of Applied Physics, USSR Academy of Sciences, on the basis of a Pulse type sensor [1, 5], was used to record the BCG. A bimorphic piezoelectric element consisting of a thin polarized piezoelectric plate served as the sensitive element. The element was soldered to a metal membrane, the thickness and strength of which were so selected as not to allow any tensile strain when bent on the soldered surface. A weight was attached to the membrane by means of a screw and it served as an inertial mass. When the sensor housing moved, the weight exerted a force on the peizelectric plate proportionate to acceleration, and this caused appearance of a charge on its facing that is proportionate to deformation, which means to acceleration as well. Sensitivity of the sensor [or transducer] is 20 $mV/m \cdot s^{-2}$. The range of working frequencies is 0.3-2000 Hz. The dimensions are 26×36×11 mm and weight is 30 g. It is contained in an ebonite housing 30×30×30 mm in size with appropriate markings. Overall weight of the BCG-1 (PAM) transducer is 60 g. It is attached to the subject with an elastic rubber strap with a metal immobilization clamp that firmly grasps the ebonite housing with sensory contained in it. This provided for uniform adherence of the sensor to the body, precluding displacement or turning during recording. The assisting crew member monitored position of the sensor in flight and the same was done on the ground by a research physician. The margin of error in applying the sensor is in the range of ±1-2 cm from the chosen point and upon repeated recording, it did not affect the amplitude-time and spectral characteristics of the BCG.

On the ground, the BCG was recorded in supine position. In weightlessness, the cosmonaut was in a free-floating state with arms and legs extended along the body during recording. The ballistocardiographic transducer was placed successively in four points of the body: in the region of the upper margin of the iliac bone, in the center of the sternum, on the back, in the interscapular region and in the sacral region. Only the longitudinal component of the BCG (along X axis) during calm breathing, as well as with breath-holding in inspiration and expiration, was recorded in the region of the superior margin of the iliac bone. In the other three points of the body, the BCG was recorded only during calm breathing, and the orientation of the transducer relative to X, Y and Z was successively changed (Figure 1).

We shall discuss here only the data obtained with the BCG recorded in the interscapular region (X, Y and Z axes). A Cardiocassette [Kardiokasseta] portable magnetic recorder was used as a recording device. The magnetic tapes were delivered to the ground for analysis under laboratory conditions. Figure 2 illustrates samples of inflight BCG tracings.

The tests were performed on three crew members of the Soviet-Indian mission six times: twice before the flight, twice during the flight (3d and 5th days of weightlessness) and twice after returning to earth (1st and 4th days).

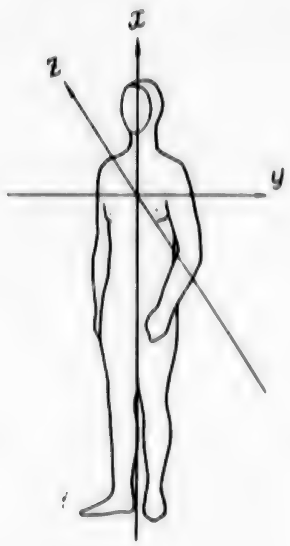

Figure 1.
Diagram of direction of axes while recording BCG

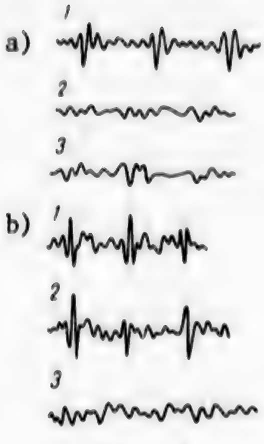

Figure 2.
Examples of BCG tracings obtained before (a) and during (b) flight on X (1), Y (2) and Z (3) axes

In addition to the usual amplitude and time analysis of the BCG, we also submitted it to spectral analysis, which consisted of isolating the spectrum of the obtained signal by expanding it in a Fourier series with analysis of frequency and amplitude characteristics of the spectrum. Spectral analysis permits detection of discrete fluctuations of biological processes and extraction of additional information from tracings obtained by the traditional method.

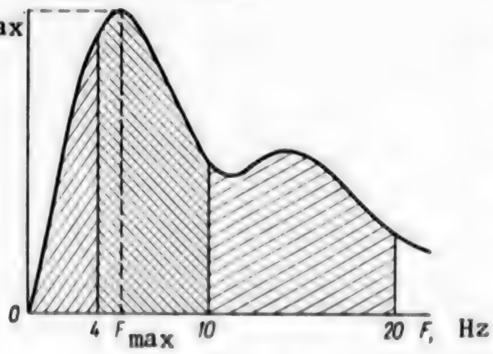

Figure 3.
Typical form of BCG spectrum. Explained in the text

Spectral analysis of the BCG was made using a special device, the SBlTs spectrobiograph which is designed to automatically process in real time the biological signals in order to obtain their amplitude and frequency spectra [6].

The ballistocardiographic signal was fed to the input of the spectrobiograph from a tape recorder. In selecting the processing mode, we took into consideration the fact that the shape of BCG complexes depends on phase of respiration, and it does not have the property of being stationary. For this reason, we chose the mode of signal accumulation for 16 s. The readings were taken in the frequency range of 0.5-62.5 Hz at 0.5-Hz intervals

The spectrobiograph effected discrete Fourier conversion by means of a digital adjustable filter. For further processing and storage, the obtained spectrum was fed into an Elektronika D3-28 computer and recorded on tape. Secondary

processing consisted of evaluating spectrum parameters. We shall discuss here the dynamics of the following spectral parameters: E_{max}--frequency of maximum harmonic of spectrum (Hz); A_{max}--amplitude of maximum harmonic of spectrum (arbitrary units), E_{0-4Hz}--total spectral energy in the frequency range of 0-4 Hz (arbitrary units), E_{4-10Hz} total spectral energy in frequency range of 4-10 Hz (arbitrary units), $E_{10-20Hz}$--total spectral energy in the frequency range of 10-20 Hz (arbitrary units).

Figure 3 illustrates schematically a typical BCG spectrum. In analyzing BCG spectra, it is expedient to examine them with consideration of the genesis of different oscillatory components. It is known that the body's oscillations are manifested in the frequency range of 4-8 Hz [2]. All oscillatory components below 4 Hz can be considered linked to the direct effect of release of blood into large vessels. The frequency and amplitude of fluctuations are determined by the mass of released blood, length and elasticity of arterial trunks (pulmonary artery and aorta), the relations between each other and to other elements of the body, in particular, the spine.

Results and Discussion

The inflight and postflight changes in amplitude-time and spectral BCG parameters were characterized by both some patterns in common and individual distinctions. We can distinguish between three variants of BCG changes. Table 1 lists the results of analysis of BCG that are typical of the first variant of changes. Here, the most marked change was increase in amplitude of IJ, JK, KL, MN segments on the 3d flight day on axis Y. A noticeable increase in amplitude of segment HI was demonstrable only on the 5th day. Power of the spectrum increases in all frequency bands on axis Z.

Table 2 illustrates the second variant of BCG changes, which is notable for the fact that there is appreciably increase in ampliutde of all BCG segments, particularly on Y and Z axes, on the 3d flight day. In this variant of BCG changes, spectrum power also increased along the Z axis at all frequency bands during flight.

With the third variant of changes (Table 3), the changes in different BCG segments on different axes did not occur at the same time. Segment HI increased on the Y axis and decreased on the X axes on the 5th day of flight. On the 3d day, segments IJ, JK and KL increase on Y and Z axes and decrease on the X axis. On the 3d flight day, the MN segment decreases on the X axis and only on the 5th day does it increase on the Z axis. Spectrum energy in the 0-4 Hz range increases distinctly in this variant on the Z axis, on the 3d day and particularly the 5th day of flight. At the same time, there is dramatic decrease in spectrum energy in the 4-10 Hz band on the X axis. Spectral power in the 10-20 Hz band increases on Y and Z axes on the 5th day of flight.

The changes in common to all these variants consisted of increase in frequency of maximum oscillation on the X axis, increased power of oscillations on the Y and Z axes in the 0-4 Hz range, as well as on all axes in the 10-20 Hz band.

Table 1. Results of amplitude and spectrum analysis of BCG with transducer placed between the scapulae (first variant of BCG changes)

Time	Axis	BCG segment, mV					Spectrum parameters				
		III	*IJ*	*JK*	*KL*	*MN*	$F_{A_{max}}$	A_{max}	E_{0-4} Hz	E_{4-10} Hz	E_{10-20} Hz
Preflight:											
I	X	0,2	0,4	0,56	0,52	0,24	6	4344	5 608	33 840	14 584
	Y	0,08	0,16	0,2	0,12	0,2	19	1376	3 082	7 684	20 258
	Z	0,12	0,2	0,36	0,36	0,16	7	1810	4 476	12 442	23 322
II	X	0,6	0,68	0,92	0,76	0,24	6	4824	6 640	44 056	15 141
	Y	0,16	0,28	0,36	0,28	0,08	7,5	1510	3 058	12 042	16 472
	Z	0,2	0,28	0,56	0,6	0,12	7,5	3624	3 984	22 804	12 736
Inflight:											
3d day	X	0,6	0,8	0,92	0,56	0,16	9,5	3952	5 620	27 980	30 524
	Y	0,16	0,72	0,84	0,44	0,42	11	4152	9 824	29 048	41 104
	Z	0,08	0,28	0,48	0,4	0,32	14	1634	6 552	13 512	20 388
5th day	X	0,28	0,92	0,92	0,44	0,44	11	3786	8 676	29 669	23 428
	Y	0,48	0,96	1,2	0,8	0,52	14	4752	13 336	33 760	38 488
	Z	0,2	0,24	0,2	0,16	0,12	18	1890	10 296	14 046	23 164
Postflight:											
1st day	X	0,62	0,24	1,6	1,26	0,3	7,5	5440	5 816	54 288	16 552
	Y	0,1	0,27	0,49	0,51	0,17	7	2800	4 128	19 884	15 732
	Z	0,13	0,44	0,87	0,72	0,16	7,5	2264	8 016	18 240	13 332
4th day	X	0,42	0,97	1,46	1,38	0,32	8	6046	5 864	57 352	17 240
	Y	0,09	0,24	0,42	0,38	0,16	5,5	1752	4 666	15 662	17 036
	Z	0,09	0,28	0,55	0,52	0,12	8	2500	4 092	18 532	14 576

Table 2. Results of amplitude and spectrum analysis of BCG with transducer placed between scapulae (second variant of BCG changes)

Time	Axis	BCG segment, mV					Spectrum parameters				
		III	*IJ*	*JK*	*KL*	*MN*	F_{A} max	A max	E_{0-4} Hz	E_{4-10} Hz	E_{10-20} Hz
Preflight:											
I	X	0,2	0,44	0,76	0,88	0,36	7,5	3136	6 968	30 608	19 644
	Y	0,08	0,16	0,12	0,2	0,08	10,5	1802	3 374	14 258	20 234
	Z	0,08	0,12	0,28	0,28	0,08	8	1684	4 988	11 496	15 202
II	X	0,32	0,64	0,8	0,76	0,2	6	3156	6 224	28 952	14 164
	Y	0,08	0,12	0,16	0,2	0,12	10,5	1856	3 950	13 482	14 970
	Z	0,08	0,16	0,32	0,2	0,2	8	2072	3 188	17 520	16 340
Inflight, 3d d	X	0,64	0,56	0,92	0,84	0,2	9,5	5680	8 408	40 440	45 776
	Y	0,4	0,72	1,08	1,04	0,8	11,5	6696	9 432	37 752	76 624
	Z	0,52	0,8	1,32	1,48	0,4	2,5	3352	17 136	31 628	42 512
Postflight:											
1st d	X	0,39	0,65	1,00	0,98	0,52	7,5	5280	5 312	35 880	25 520
	Y	0,12	0,19	0,31	0,41	0,19	9	2784	3 288	15 684	20 828
	Z	0,23	0,32	0,4	0,25	0,16	4,5	6696	9 432	37 752	76 624
4th d	X	0,28	0,28	0,57	0,61	0,31	7	5656	7 048	41 736	26 384
	Y	0,27	0,36	0,37	0,28	0,09	7,5	1962	5 156	19 920	19 782
	Z	0,16	0,28	0,52	0,52	0,32	7,5	3480	3 372	22 328	26 488

Table 3. Results of amplitude and spectrum analysis of BCG with transducer placed between scapulae (third variant of BCG changes)

Time	Axis	BCG segment, mV					Spectrum parameter				
		HI	*IJ*	*JK*	*KL*	*MN*	$F_{A_{max}}$	A_{max}	E_{0-4} Hz	E_{4-10} Hz	E_{10-20} Hz
Preflight:											
I	*X*	0,32	0,8	1,2	0,92	0,4	5	4720	6 176	37 456	15 840
	Y	0,16	0,12	0,2	0,36	0,12	4,5	4088	14 346	15 524	16 136
	Z	0,16	0,24	0,12	0,2	0,08	10,5	1732	4 116	10 554	12 144
II	*X*	0,28	0,68	0,96	0,72	0,4	5,5	5200	7 280	37 176	11 768
	Y	0,08	0,2	0,32	0,2	0,12	11,5	1856	4 828	13 966	14 834
	Z	0,04	0,08	0,16	0,16	0,08	6,5	1168	4 022	10 006	10 031
Inflight:											
3d day	*X*	0,16	0,32	0,56	0,32	0,12	9,5	1642	4 844	13 032	12 178
	Y	0,08	0,32	0,48	0,44	0,16	9,5	2384	4 252	17 568	19 408
	Z	0,08	0,16	0,24	0,24	0,12	6,5	1864	5 082	10 820	12 882
5th day	*X*	0,18	0,44	0,68	0,48	0,24	8,5	1784	5 046	18 246	14 218
	Y	0,24	0,4	0,32	0,20	0,12	9,5	1854	4 890	15 574	20 240
	Z	0,12	0,24	0,32	0,16	0,16	11,5	1548	6 216	12 624	20 926
Postflight:											
1st day	*X*	0,27	0,51	0,71	0,64	0,28	6,5	4036	3 156	27 376	8 228
	Y	0,09	0,27	0,40	0,32	0,13	11,5	2552	4 935	12 208	16 040
	Z	0,16	0,31	0,25	0,09	0,08	11,5	2612	4 752	16 376	23 056
4th day	*X*	0,28	0,56	0,69	0,61	0,29	6	5264	5 288	30 424	11 200
	Y	0,09	0,27	0,32	0,11	0,07	11	3004	3 820	14 929	13 084
	Z	0,13	0,23	0,21	0,09	0,09	10,5	1474	2 818	12 450	12 486

The findings indicate that the energy of mechanical function of the heart is redistributed in flight. The increase in energy of oscillations on the Y (1st and 2d variants of changes), as well as Z (3d variant) axes and decrease on the X axis are apprently attributable to intensification of activity of the right heart due to increased amount of blood in the pulmonary vessels and elevation of pressure in the pulmonary artery. The individual distinctions of anatomical structure and location of major arterial trunks affect processes of transmission and dissipation of mechanical energy of cardiac contractions. For this reason, the nature of changes in segments of the spatial BCG and spectra differed in crew members. The rate of change in hemodynamics to a new functional level also differed. Thus, in the second variant, there were distinct differences in the spatial BCG, as compared to the baseline, already on the 3d flight day, whereas in the third variant changes appeared only on the 5th day. In the second variant, there is good demonstration of the sequence of changes, first in external function of the heart (changes in segments IJ, JK, KL on the 3d flight day), then in functional state of the myocardium (change in segment HI on the 5th flight day).

The noticeable increase in energy of oscillations in the 10-20 Hz band is indicative of the fact that the observed changes in the spatial BCG are related mainly to redistribution of blood to the upper half of the body, in particular, to increased blood in the lungs. The shift of maximum energy in the frequency range above 10 Hz is only partially related to disappearance of resonance oscillations of the entire body with retention of mutual oscillations of its different parts. These oscillations also exist on the ground, and there is no reason for their energy to increase significantly in weightlessness. The

fact that there is greater increase in oscillation energy in the 10-20 Hz band on the Y and Z axes warrants the belief that additional blood in the pulmonary vessels may be the source of such oscillations. Along with elastic "suspension devices" (alveolar tissue, mediastinum, large vessels) these amounts of blood generate numerous local oscillatory systems expressly in the Y-Z plane.

The increase in energy of oscillations on Y and Z axes in the 0-4 Hz frequency band is an important scientific fact. These frequencies reflect the actual force of cardiac contraction, they characterize external function of mainly the right heart.

Thus, for the first time direct evidence was obtained of an increase in mechanical activity of the right ventricle in the acute period of adaptation to microgravity. Redistribution of energy of cardiac contractions in the right and left chambers is one of the elements of change in central hemodynamics attributable to changes in pressure and volume in systemic and pulmonary circulation. Such change occurs at a different rate and in a dissimilar sequence in different people, which explains the different variants of changes. Thus, in the second variant, the 5.5-fold increase in energy of the spectrum on the Z axis in the 0-4 Hz frequency band was observed already on the 3d flight day. In the third variant, a 1.5-fold increase in energy was noted only on the 5th day of flight. No specific postflight changes were demonstrable. For 1 day there were still many of the spectral distinctions discovered in flight. On the 4th postflight day, the BCG corresponded essentially to preflight tracings.

The data obtained of changes in parameters of spatial ballistocardiography in members of the Soviet-Indian crew demonstrate the existence of objective changes in cardiac contractility at the early stage of adaptation to weightlessness. There is every reason to assume that further development of spatial ballistocardiography will permit not only gaining more definite information concerning some important problems of pathogenesis of hemodynamic changes during spaceflights, but use of this method to solve practical problems of medical monitoring.

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COSMONAUTS' HORMONAL RESPONSES AFTER BRIEF SPACEFLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 16 May 83) pp 32-35

[Article by R. A. Tigranyan, N. F. Kalita, T. A. Kiseleva, V. M. Ivanov, Ye. V. Kolchina and B. V. Afonin]

[English abstract from source] After short-term (7-day) space flights the following parameters were measured in blood of cosmonauts: cortisol, ACTH, aldosterone, thyrotropic hormone, thyroxine, triiodothyronine, somatotropic hormones, insulin, testosterone, cyclic nucleotides, prostaglandins, activities of the kallikrein-kinin, fibrinolytic and coagulatory systems, and plasma renin activity; in addition, renal excretion of aldosterone and total 17-oxycorticosteroids was determined. It was demonstrated that after the shoft-term flights the acute period of adaptation was accompanied by a moderate activation of the renin-angiotensin-aldosterone system, adrenal glucocorticoid function, pancreatic insular apparatus, kallikrein-kinin system as well as increased cyclic AMP which is suggestive of a moderately expressed stress reaction.

[Text] The neuroendocrine system plays an important part in formation of homeostatic adaptive reactions to spaceflight factors and, during subsequent recovery, to earth's gravity [5]. The results of biochemical tests performed after each spaceflight represented a complicated picture of diverse, sometimes contradictory changes in most blood and urine parameters, as compared to the preflight status. Here, the distinctions of cosmonauts' individual responses to space factors could have had some significance.

Our objective here was to study the hormonal status and activity of the kallikrein-kinin (KKS), clotting and fibrinolytic systems of cosmonauts who had participated in 7-day spaceflights, as well as to determine the nature of stress reaction in the acute period of readaptation to earth's gravity. Statistical analysis of the aggregate of data obtained in missions of the same duration will enable us to assess with greater reliability the patterns of responses to brief weightlessness.

Methods

Venous blood and 24-h urine served as material for our studies. Conclusions pertaining to the main regulatory systems of cosmonauts were based on comparison of results of preflight and postflight biochemical tests performed with the participation of 17 cosmonauts who had made 7-day flights aboard spacecraft of the Soyus and Soyuz-T series. The following served as baseline parameters: results obtained 30-40 days prior to the missions for blood tests, those obtained 30, 29, 28, 5, 4, 3 days before the missions for urinalyses. Postflight examination on the 1st and 7th days after landing consisted of the following: collecting 24-h urine on the day of landing (0 day) and for the next 5 days. Radioimmune analysis was used to assay levels of cortisole, adrenocorticotropic hormone (ACTH), insulin, aldosterone, thyrotropic hormone (TTH), thyroxine (T_4), triiodothyronine (T_3), testosterone, cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP), prostaglandins (PG) of pressor (PG $F_{2-\alpha}$) and depressor (PG A+E) groups, as well as plasma renin activity. Parameters characterizing KKS (baseline arginine-esterase activity, prekallikrein content and activity of its inhibitor), clotting (prothrombin content and activity of its inhibitor) and fibrinolytic (plasminogen content and activity of its inhibitor) systems of blood were tested only on the 1st postflight day by a method that was previously published [2]. Aldosterone content of urine was determined by radioimmune analysis and excretion of total 17-hydroxycorticosteroids (HCS) by the reaction with phenyl hydrazine [7].

The obtained results were submitted to variation statistical processing with use of the Fisher-Student criterion.

Results and Discussion

Preflight changes were found in the cosmonauts in the correlation between pressor and depressor PG, as well as high ACTH content (at the top of the normal range) of blood (Table 1), which is typical of emotional stress [10]. Excretion of HCS in urine increased in both the baseline (above normal) and prelaunch periods (Table 2), which is also typical of emotional tension. The observed changes are most probably due to the cosmonauts' reactions to different tests and loads during the clinicophysiological examination, as well as emotional tension related to preparations for the mission.

Blood cortisol content increased reliably on the 1st and 7th postflight days (see Table 1); however, no other signs of activation of the hypophysis-adrenocortical system were demonstrable. Blood ACTH concentration (see Table 1) and excretion of total HCS in urine (see Table 2) were on the level of preflight values. However, it should be noted that at both postflight tested times HCS levels, as well as excretion in urine of total HCS on the 1st postflight day, were above normal. In all likelihood, the significant scatter of individual values for excretion of total HCS in urine and blood ACTH content in the postflight period did not permit demonstration of reliable changes in these parameters; however, in a number of instances we demonstrated values for these parameters that exceeded the normal range, particularly with respect to total HCS content of urine [3].

Table 1. Levels of hormones and biologically active compounds in cosmonauts' blood (M±m)

Parameter	30th Preflight day	Postflight day	
		1	7
ACTH, pg/mℓ	50,48±10,12	60,53±5,34	71,90±16,81
Cortisol, μg%	12,39±1,82	20,39±0,83*	20,85±1,29*
Renin, ng/mℓ•h	2,25±0,38	4,30±0,57*	2,26±0,64
Aldosterone, pg/m	46,8±5,2	80,0±7,8*	57,7±15,4
Insulin, μU/mℓ	11,46±0,94	15,17±1,06*	20,09±1,34*
TTH, μU/mℓ	1,60±0,20	1,56±0,12	1,24±0,33
T_4, μg%	7,18±0,59	8,65±0,49	8,41±0,47
T_3, ng%	148,5±10,6	161,2±6,7	122,3±18,5
STH, ng/mℓ	1,81±0,56	2,08±0,13	2,76±0,17
Testosterone, ng%	579,6±56,2	563,3±67,6	516,6±50,9
cAMP, pk[?]mol/mℓ	14,7±4,7	31,1±4,6*	13,2±3,5
cGMP, pkmol/mℓ	4,2±1,1	6,7±0,9	4,5±1,2
PG A+E, ng/mℓ	2,37±0,51	1,34±0,33*	2,14±0,69
PG F_2-α, ng/mℓ	1,95±0,19	0,62±0,2[illegible]	0,82±0,26
[NB: pk could be typo for micro or pico]			

*Here and in Tables 2 and 3: reliable differences as compared to preflight values.

Table 2. Excretion in urine of steroid hormones (M±m)

Parameter	Preflight day		Postflight day					
	30	3—5	0-day	1	2	3	4	5
Total HCS, mg/d	7,11±2,00	6,99±1,81	5,21±0,86	8,13±1,15	6,91±1,21	7,29±2,12	5,99±1,04	6,41±0,96
Aldosterone, μg/day	12,6±1,9	16,6±2,1	14,4±1,4	20,8±2.4*	18,7±2,3*	21,3±2,0*	20,3±3,9	11,2±2,1

Thus, elevation of parameters characterizing glucocorticoid function of the adrenals on the 1st postflight day could be indicative of its moderate activation, which should be interpreted as the result of nervous and emotional tension related, in particular, to successful completion of the space mission.

At the present time, it is believed that readaptation to conditions on the ground after exposure to weightlessness is associated with a strain of at least the cardiovascular and muscular systems, which is inevitably associated with activation of adrenal glucocorticoid function. However, as shown by the results of studies, following completion of short-term spaceflights thereis not always increase in excretion of total HCS in urine, which served as the basis for expounding the conception of postflight functional hypoadrenocorticism [1]. It was shown that adrenocortical dysfunction, manifested by a relative hydroxylation deficiency during synthesis of corticosteroids, may be the cause of intact excretion of total HCS in response to gravity stress [8, 9].

Table 3.
Activity of kallikrein-kinin, fibrinolytic and clotting systems of cosmonauts' blood (M±m)

Parameter	30th Preflight d	1st Postflight d
Baseline arginine-esterase activity, μmol/mℓ•h	3,86±0,20	5,44±0,60*
Prekallikrein, μmol/mℓ•h	62,3±3,4	49,1±1,2*
Kallikrein inhibitor, units	0,9±0,04	0,8±0,03*
Plasminogen, μmol/mℓ•h	66,7±1,2	63,6±1,3
Plasmin inhibitor, units	0,18±0,03	0,24±0,03
Prothrombin, μmol/mℓ•h	63,9±2,3	58,6±3,5
Thrombin inhibitor, units	1,08±0,05	1,02±0,07

On the other hand, the response of the adrenal cortex to change from weightlessness to earth's gravity depends largely on individual distinctions [8, 9].

On the 1st postflight day, there was noticeable activation of the renin-angiotensin-aldosterone system (RAAS), as indicated by the reliable increase in plasma renin activity (beyond the normal range), elevation of blood aldosterone level (see Table 1) and its increased excretion in urine for the first 3 postflight days (see Table 2). Emotional tension [10] and loss of fluid and electrolytes during spaceflight could be the cause of such increase in RAAS activity. These changes can be interpreted as being directed toward restoring fluid-electrolyte changes arising in cosmonauts during flights.

In the postflight period there was distinct stimulation of β-cells of the islet system of the pancreas, as manifested by reliable elevation of blood insulin level at both tested times (see Table 1), which could also be indicative of a stress reaction since insulin, along with other hormonal parameters, is a system that realizes the effects of catecholamines. A moderate stress reaction also determines the status of metabolic processes in cosmonauts in the acute recovery period following short-term spaceflights. We have shown that there is elevation of blood glucose level [6] in the acute period of recovery, and it was compensated by an increase in blood insulin content. Evidently, the increase in blood insulin concentration could also be due to increased epinephrine in blood, which was noted in cosmonauts at these test times [6]. This could cause accumulation of triglycerides in blood of cosmonauts who participated in short-term spaceflights [4].

The reliable elevation of blood cAMP level on the 1st day of the recovery period could be due to release of various hormones into blood and be indicative of stress during this period [10].

Investigation of blood levels of both groups of PG revealed that the observed reliable decline (below normal) of PG A+E on the 1st postflight day, which caused an increase in the ratio of PG pressor to depressor components, is a reaction to prevent orthostatic instability and retention of sodium, and it may be indicative of presence of nervous and emotional tension.

On the 1st postflight day, there was appreciable activation of KKS, which is confirmed by the reliable decrease in prekallikrein content and activity of kallikrein inhibitor, with concurrent reliable increase in initial arginine-esterase activity (see Table 3). It is known that a hemodynamic depressor effect is one

of the manifestations of KKS activity. Acting in coordination and equilibrium with pressor systems (catecholamines, glucocorticoids, mineralocorticoids, renin, PG pressor group), this system helps the body adapt faster to earth's gravity.

The other tested parameters of cosmonauts' blood showed only insignificant differences from the preflight levels.

Thus, the acute recovery period for cosmonauts who participated in 7-day spaceflights was associated with a moderate stress response, as indicated by activation of glucocorticoid function of the adrenals, β-cells of the pancreatic islet system, RAAS, change in relationship between PG pressor and depressor groups, elevation of blood cAMP "second messenger" level, as well as activation of KKS. The observed changes were apparently caused by the physiologically validated need to maintain homeostasis under the unique conditions of spaceflight and in the period of readaptation to earth's gravity. We failed to demonstrate any signs of marked changes in the basic regulatory systems of cosmonauts in the acute recovery period.

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HUMAN AND ANIMAL HYPOVOLEMIC REACTIONS TO INCREASING +Gz ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 14 May 86) pp 35-39

[Article by R. A. Vartbaronov, G. D. Glod, N. N. Uglova and I. S. Rolik]

[English abstract from source] Maximal variations of the circulating blood and plasma volumes after water load and/or exposure to increasing +Gz were investigated in manned and animal studies. The animal study demonstrated that the relative changes in the circulating blood and plasma volumes can be calculated using hematocrit or hemoglobin values. On the 2d minute after exposure to increasing +Gz of up to 14.5G the animals showed a decrease (by 11.7%) of the circulating blood volume which was primarily associated with plasma losses. The change was not appreciably modified by the use of an anti-G suit. In the manned studies the decrease was 5.9% during exposure to 7 G and 11% during exposure to 9 G with an anti-G suit used. These observations show that the acceleration duration and value play an an important part in the mechanism of plasma filtration in response to an increase in the hydrostatic pressure.

[Text] It was previously established [4] that phasic adaptation states, including a phase of cumulative effects, are inherent in the repeated effects of exposure to +Gz accelerations. The possible cause of development of this phase could be hypovolemia, which occurs due to filtration of liquid part of blood into the extravascular space as a result of prolonged elevation of hydrostatic pressure. In some works [9, 10, 12, 14-18], it was shown that there is reliable relative decline in circulating plasma (CPV) and blood (CBV) volume in man and animals after exposure to accelerations of 2.5-10 G lasting for up to 30 min. In other studies, in which exposure did not exceed 1.5 min, no changes were found in blood hematocrit or hemoglobin concentration [13].

A comparative study was made of hypovolemic responses in man and animals, which arose under the effect of repeated exposure to +Gz of increasing intensity, with or without wearing a G suit, in order to further explore this matter.

Methods

The studies were conducted on 5 adult mongrel dogs weighing 6-10 kg and with participation of 5 healthy men 20-25 years of age. In order to validate the feasibiligy of using hematocrit or hemoglobin parameters to calculate the relative changes in CPV and CBV in man and animals, a model of short-term hyperhydration was produced by means of a water load. For this purpose, dogs were fed a meat broth in amounts of 3-4% of their weight, which was stimulated by depriving the animal of a scheduled mealtime and water intake on the day before the experiment. Against such a background, hematocrit tests failed to reveal signs of dehydration. Intake of broth (rather than water) made it possible to extend subsequent hyperhydration to 2-2.5 h. In order to produce a water load in man, we used tap water that was given to the subjects in amounts of 1% of their weight. We measured concentration of hemoglobin and hematocrit in the animals [6] and only hemoglobin concentration, using the acetone cyanohydrin method, in man [3]. Measurements were taken before fluid intake and every 15 min thereafter for 1.5-2 h.

The method of immobilizing animals on the centrifuge, their prepration as well as modes of exposure were described previously [2]. Repeated exposure to increasing +Gz accelerations was continued until the animals presented marked disturbances of cardiac rhythm [1]; for man, exposure was continued until there was appearance of visual disorders of the "gray veil" type.

The modes of exposure in the tests with man were continuous and consisted of "plateaus" lasting 30 s each for increasing accelerations of 3, 5, 6 and 7 G without a G suit and 3, 5, 6, 7, 8 and 9 G with the suit. The rate of build-up of +Gz constituted 1 G/s; the acceleration level was dropped to 2 G for 15 s in the intervals between plateaus. Hematocrit was measured in dogs and hemoglobin concentration in the men 10-15 min before exposure and 2 min after it.

Thereafter, the hemoglobin and hematocrit values were used to calculate the relative changes in CBV and CPV using formulas that assume there are no reliable changes in hemoglobin mass [8, 9, 12, 14, 16]:

$$\Delta PV_1 = \frac{100 \cdot 100(Hct_0 - Hct_1)}{(100 - Hct_0) \cdot Hct_1}, \quad (1)$$

$$\Delta PV_2 = 100 \frac{Hb_0}{Hb_1} \cdot \frac{1 - 0{,}01\,Hct_1}{1 - 0{,}01\,Hct_0} - 100, \quad (2)$$

$$\Delta PB = 100 \cdot \frac{Hb_0}{Hb_1} - 100, \quad (3)$$

where Hct_0, Hct_1 is hematocrit (%) before and after exposure; Hb_0, Hb_1 is concentration of hemoglobin (g%) before and after exposure; ΔPV_1 and PV_2 is relative change in CPV (%) calculated from Hct and Hct+Hb parameters, respectively; ΔPB is relative change in CBV (%) calculated using Hb [8].

The obtained data were submitted to statistical processing by methods of regression and correlation analysis [7].

Results and Discussion

A high correlation (R = 0.95) was demonstrated between Hb and Hct measured in the same blood sample from animals with and without short-term water load (Table 1). Random error constitutes only ±5.5%. The unreliable change in red cell volume after the water load, which constituted +5±4.1%, may be considered the most likely cause of the high correlation. As a result of this correlation, the relative changes in CPV calculated using formulas 1 and 2 were also similar, and the systematic and random errors constituted about 6% (formula 6).* Analogous relations were found in man (formula 7).

Table 1. Regression functions for hematocrit, hemoglobin concentration and estimated relative changes in CPV and CBV in dogs

	Regression equations	*n*	Estim. regress.	Random error, %	Coeffic. of correlation (R)	Systemic error, %
4	$Hb = 0.3Hct + 1.0$	34	0,72 g%	5,4	0,95	
5	$Hct = 3 \cdot Hb + 1.3$	34	2,3	5,5	0,95	
6	$\Delta PV_1 = 0.82 \cdot \Delta PV_2 - 0.6$	20	6,3	6,3	0,92	5 – 6
7	$\Delta PV_1 = 0.87 \cdot \Delta PV_2 - 1.29$	45	Accord. to literature			
8	$\Delta PB = 0.7 \cdot \Delta PV_1 + 1.8$	20	9,0	9,0	0,82	2,5
9	$\Delta PV_2 = 1.37 \cdot \Delta PB + 1.8$	20	4,6	4,6	0,98	–

Note: Here and in Tables 2 and 3, *n* refers to number of measurements. Calculation of CPV changes using formula (7) was made only for man [12].

Table 2. Maximum changes in relative plasma and blood volumes 30-60 min after water load (WL)

Subject	*n*	Time	Hb, %	Hct, %	ΔPV, %	ΔPB, %
Animals	13	Baseline	—	49,4±1,35	—	—
		After WL	—	43,9±1,61*	25,1±4,7**	12,3±2,5**
Man	7	Baseline	15,0±0,22	—	—	—
		After WL	14,2±0,24	—	9,5±1,6**	5,2±0,9**

Note: Here and in Table 3, * $p \leq 0.05$, ** $p \leq 0.01$.

Thus, one can calculate relative CBV changes only according to hematocrit (formulas 1 and 8), and relative changes in CPV only according to hemoglobin concentration (formulas 3 and 9).

In man, a 1% water load elicits reliable increase in CPV and CBV, which is considerably less marked than the effect of a 3-5% water load on animals (Table 2). The relative increment of CPV is 1.8-2.0 times greater than that of CBV, which is indicative of insignificant change in erythrocyte volume

*Formulas 4-9 are given in Table 1.

Table 3. Change in relative plasma and blood volumes under effect of repeated exposure to increasing +Gz accelerations (M±m)

Subject	G suit	Accel. parameters: maximum G	Accel. parameters: duration, min	Testing time	HB, %	Hct, %	ΔPV, %	ΔPB, %
Animals	Not used (10)	14,4±0,7	6,8±0,6	Before exposure	—	48,1±1,7	—	—
				After "	—	55,0±1,8**	−23,2±2,6**	−11,7±1,4**
	Used (4)	14,5±1,3	6,9±1,1	Before "	—	50,1±2,3	—	—
				After "	—	56,9±3,4	−23,6±4,5**	−11,2±1,8**
Man	Not used (7)	7,0	3,3±0,3	Before "	15,8±0,5	—	—	—
				After "	16,8±0,5	—	−11,1±4,0*	−5,9±2,1*
	Used (11)	9,0	5,7±0,2	Before "	15,3±0,7	—	—	—
				After "	17,3±0,5**	—	−20,5±40**	−11,0±2,1**

Note: Number of animals is given in parentheses.

after the water load not only in animals, but in man. Thus, with the water load the changes in CBV occur due to increase in CPV. An analogous situation (although the CBV changes are in the opposite direction) is observed under the effect of +Gz, including instances where it is combined with a water load, when the increase in red cell volume does not exceed 2% [12, 13]. These results are indicative of the feasibility of using hematocrit or hemoglobin parameters separately to measure relative CBV and CPV.

In our studies, the relative decrease in CBV after repeated exposure to accelerations of increasing intensity was less marked than for CPV (Table 3). Consequently, the relationship between absolute (without consideration of sign) values for these parameters was about the same as with a water load (see Tables 2 and 3). On the other hand, since the level of accelerations to which animals were exposed with and without use of G suit were the same, it can be assumed that the decrease in relative CPV and CBV in these tests was unrelated to use of the G suit. As for reliable differences in CBV changes obtained in the tests on man (see Table 3), they were apparently attributable to the difference in level and time of exposure to accelerations. CPV and CBV parameters reverted to baseline values by the 40th-50th min of the aftereffect period [12, 14].

Thus, the results of these studies revealed that decrease in CBV may be one of the possible physiological mechanisms of onset of the phase of cumulative effects of repeated accelerations. If we consider 5 ℓ as the baseline CBV for man, the estimated loss of CBV in the series with use of the G suit would be 0.55 ℓ, which may have an appreciable effect on tolerance to repeated exposure to accelerations [12]. Figures cited in other works for the relative decrease in human CBV are close to our data [12, 14, 15]. Duration and magnitude of accelerations are of the greatest relevance. This mechanism is not specific to head-pelvis accelerations, since similar hypovolemic reactions were demonstrated in tests on animals with pelvis-head accelerations [11]. These reactions are inherent not only in repeated

but continuous exposure to accelerations for a long time (several minutes), and they should be associated with subsequent triggering of the antidiuretic mechanism that has been established for long-term orthostatic position and head-pelvis accelerations [5, 11, 12, 15]. Since this adaptive mechanism has a long latency period (several min) and is the consequence of hypovolemic reactions [12, 14, 15], we shall not deal with it here.

In conclusion, it should be stressed that the filtration-dehydration mechanism in itself cannot be viewed solely from the standpoint of adverse effect of accelerations. The rapid passage of plasma into the interstitial space apparently fails to be compensated by efflux of lymph, which is also more difficult with exposure to accelerations, which leads to elevation of intratissular pressure, thereby creating a sort of antigravity effect. Cumulative phenomena most probably appear at the late stage of filtration when plasma loss reaches a critical level. Determination of these correlations could be the subject of future investigations.

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KARYOMETRIC EVALUATION OF NEURONAL REACTIONS OF RAT CEREBRAL CORTEX TO THE COMBINED EFFECT OF IONIZING RADIATION, LONGITUDINAL ACCELERATIONS AND VIBRATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHFSKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 19 Aug 86) pp 39-42

[Article by V. P. Fedorov and I. B. Ushakov]

[English abstract from source] Using karyometric procedures, the reactions of neuronal nuclei of the middle layers of the sensorimotor cortex of rats exposed to the combined effect of ionizing radiation and longitudinal acceleration or vertical vibration were investigated. It was found that the size of neuronal nuclei varied depending on the radiation dose and type of combinations of radiation with other exposures.

[Text] The combined effect of flight factors on the central nervous system is one of the problems of aviation and space medicine [1]. Nucleus volume is one of the tests to assess neuronal function, intensity of neuronal metabolic processes and permeability of cell membranes. There are only isolated works in the literature dealing with karyometric characterization of central nervous system responses to ionizing radiation [5-7], vertical rotation [9, 10], horizontal rotation [3] and vibration [11]. There is absolutely no information about the combined effect of these factors on neurocyte nuclei. For this reason, our objective here was to assess the changes in neuronal nuclear volume in the rat sensorimotor cortex under the combined effect of radiation and dynamic flight factors. For karyometric analysis, we used neurons of the 3d and 4th cortical layers (fields FPa, FPp and PAs on the map of V. M. Svetukhina), which receive afferent impusation and perform higher associative and analytical functions.

Methods

These studies were conducted on Wistar rats weighing 200-220 g, whose head was exposed to γ-radiation in doses of 10, 50 and 200 Gy at a dose rate of 12 cGy/s. The animals were exposed to longitudinal "head-pelvis" (+Gz) acceleration of 5 G for 2.5 min (build-up gradient 0.25 G/s), as well as vibration for 1 h at build-up of 8 m/s^2 at a frequency of 80 Hz, which is the most significant for the central nervous system [8], prior to or immediately following irradiation. There was a 15 min interval between the factors. Animals exposed to "pseudo

radiation" with prior or subsequent immobilization on the centrifuge or vibration table served as a control. There were six animals in each experimental group. The material (segments of sensorimotor cortex) was collected after decapitating the animals, 1.7 h after irradiation; it was fixed in Carnoy fluid and, using dioxane, imbedded in paraffin. Diameters of nuclei in the 3d and 4th layers of the sensorimotor cortex were measured on 6-μm sections stained after Nissle, using a screw-type ocular MOV-1-15* micrometer at a magnification of 2025×. The obtained data were converted to micrometers and, using the formula for ellipsoid rotation ($V = 1/6 \cdot \Pi \cdot \alpha \cdot \beta^2$, where α is the larger and β is the smaller diameter of a nucleus) and the table in [4], we determined the nucleus volume. Then logarithms were taken of nuclear volumes in cubic micrometers, and they were combined into groups at 0.1 class intervals, and determination was made of the percentage of each class in all animals of each experimental group to plot variation curves. The obtained data were submitted to the usual statistical processing.

Results and Discussion

The studies revealed that brief exposure to longitudinal accelerations did not elicit significant changes in karyometric parameters after 1.7 h. The variation curve of incidence of logarithm classes virtually coincided with the one for control animals (Figure 1).

Radiation elicits some decrease in nucleus volume with a left shift of the variation curve due to increase in number of nuclei with less than 1.9 volume logarithm and decrease in number of larger nuclei. Prior centrifuging led to the finding that karyometric postradiation parameters virtually failed to differ from the control. As in the control, the largest number of nuclei are referable to the logarithm classes of 1.8-2.1. If, however, the rats were submitted to acceleration after irradiation, in spite of an unchanged mean volume, the variation curve remained shifted to the left due to increase in number of nuclei with a logarithm of less than 1.9 and decrease in number of larger nuclei.

Thus, brief exposure to head-pelvis accelerations prior to irradiation elicits "normalization" of karyometric parameters. Exposure to accelerations following radiation causes a decrease in volume of nuclei and in their functional activity.

Vibration at a frequency of 80 Hz elicits shriveling of nuclei ($p<0.05$), as compared to the control, which causes a left shift of the variation curve of volume logarithms (Figures 2-4).

Exposure of the rat head to 10 Gy radiation did not elicit changes in average volume of nuclei after 1.7 h, while the variation curve of their distribution in logarithm classes virtually coincided with that of control animals (see Figure 2).

When rats were submitted to vibration after irradiation, neurocyte nuclei decreased in volume, as compared to both the control and irradiation. The variation curves of their distribution in classes shifted to the left due to increase in volume of nuclei of less than 1.9 class and significant decrease in number of nuclei of "higher" classes.

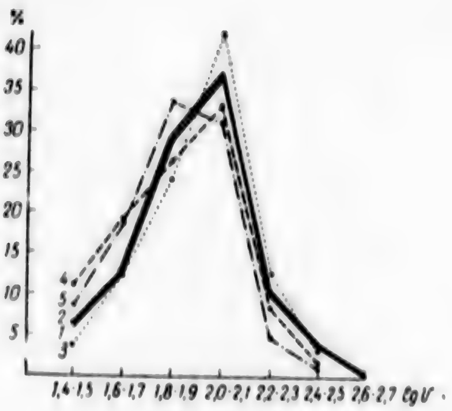

Figure 1.
Variation curves of distribution of neurocyte nuclei of rat sensorimotor cortex according to logarithm classes after exposure of the head to 50 Gy radiation combined with longitudinal head-pelvis accelerations

1) intact group
2) accelerations
3) accelerations + radiation
4) radiation + accelerations
5) radiation

Here and in Figures 2-4: X-axis, logarithms of nucleus volumes; y-axis, percentage of nuclei of a given class encountered.

Figure 2.
Variation curves of distribution of neurocyte nuclei of rat sensorimotor cortex in logarithm classes after exposure of head to 10 Gy radiation combined with vibration

1) intact group
2) vibration
3) radiation
4) radiation + vibration
5) vibration + radiation

When vibration preceded irradiation, the variation curve of distribution of nuclei in logarithm classes was virtually the same as with irradiation alone.

Thus, vibration preceding exposure of the head to 10 Gy radiation had no appreciable effect on karyometric parameters. However, if the animals were submitted to vibration after radiation, the nuclei had a tendency toward shriveling. It should also be noted that the karyometric parameters were closer to control values than to those with vibration alone in all of the experimental groups.

The findings were somewhat different with a large dose of ionizing radiation (see Figure 3). Thus, exposure of the rat's head to 50 Gy radiation elicits, after 1.7 h, some increase in functional activity of neuronal nuclei in the sensorimotor cortex, as manifested by a right shift of the variation curve. At the same time, the mean volume of nuclei changed unreliably. When rats were submitted to vibration after radiation, the nuclei showed a dramatic reduction in volume ($p<0.05$), as compared to both the control and radiation alone. The variation curve was in the far left position, even further left than with use of vibration alone. When vibration preceded radiation, the volume of nuclei was also smaller ($p<0.05$) than in the control animals or those exposed to

radiation alone. The variation curve of distribution of nuclei in logarithm classes was also shifted to the left, but now this was in comparison to the effect of vibration alone, as well as the group of animals submitted to vibration following radiation. There was an overt tendency toward its normalization. Thus, the largest number of nuclei was referable to the 1.8-1.9 logarithm class, as in control animals. We see that vibration, both before and after delivery of 50 Gy radiation to the head, elicits wrinkling of nuclei, and in this respect vibration had the most adverse effect on irradiated animals.

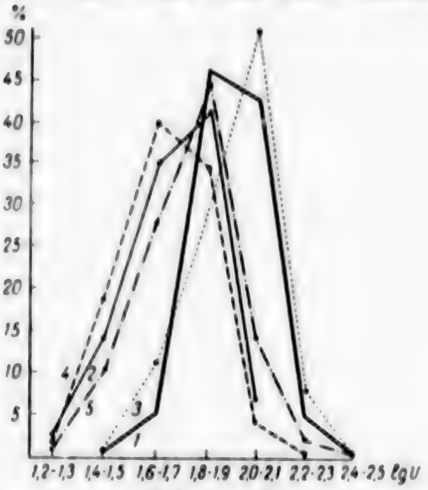

Figure 3.
Variation curves of distribution of neurocyte nuclei of rat sensorimotor cortex in logarith classes after exposure of the head to 50 Gy radiation combined with vibration

1) intact group
2) vibration
3) radiation
4) radiation + vibration
5) vibration + radiation

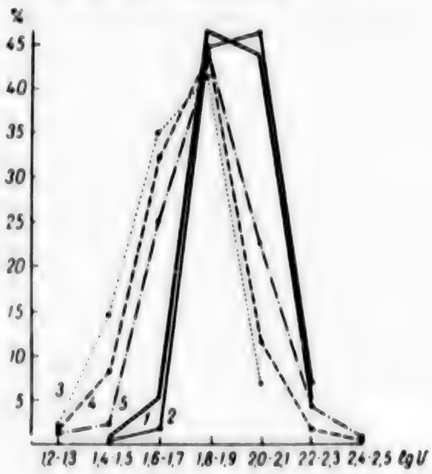

Figure 4.
Variation curves of distribution of neurocyte nuclei of rat sensorimotor cortex following exposure of the head to 200 Gy radiation combined with radiation

1) intact group
2) vibration
3) radiation
4) radiation + vibration
5) vibration + radiation

Delivery to the head of radiation in a dosage of 200 Gy 1.7 h after exposure to vibration virtually failed to change the volume of neurocyte nuclei in the central layers of the sensorimotor cortex. The variation curve of distribution of nuclei in logarithm classes was virtually the same as in control animals (see Figure 4). Here we see some "areactivity" of this parameter when the intensity of exposure goes beyond a certain limit. When rats were submitted to vibration after radiation, the nuclei decreased significantly in volume ($p<0.05$) as compared to both the control and the irradiated group of animals. The variation curve of distribution of nuclei in logarithm classes shifted to the left, but did not exceed the range observed with vibration alone. With exposure to vibration prior to radiation, the nuclei also diminished in volume ($p<0.05$), as compared to the control and irradiated groups of animals. However, this schriveling was less marked than with use of vibration after irradiation of the head.

Thus, the combination of γ-radiation delivered to the rat head in a dosage of 200 Gy and vibration leads to shriveling of nuclei and, consequently, to

their loss of cellular fluid and decrease in functional activity. More marked changes are demonstrable in the group of animals submitted to vibration following radiation.

Let us note that the general principles of radioresistance to the combined effect of ionizing radiation and dynamic flight factors were demonstrated previously [2]. However, while in the cited work there was discussion mainly of the hemopoietic system as the "acceptor of radiomodification," in our study we were dealing with the central nervous system exposed to the factors on three dose levels.

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BLOOD REDISTRIBUTION IN MAN WITH LOWER BODY NEGATIVE PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 15 Apr 86) pp 42-45

[Article by V. A. Degtyarev, M. A. Kaplan, L. Ya. Andriyako, Yu. A. Bubeyev and Yu. I. Remizov]

[English abstract from source] During exposure to LBNP of -10 to -60 mm Hg variations in the blood filling of body segments were measured, using ^{59}Fe labelled erythrocytes. The study was performed on 10 healthy volunteers each of which was exposed to six LBNP sessions (in recumbency). The data obtained were related to changes in the blood filling of various body segments (head, thorax, abdomen, pelvis, legs) which were the most pronounced at LBNP -20 to -30 mm Hg. As the LBNP level increased, the changes in the blood filling of the pelvis and legs, head and thorax decreased. In the abdominal area this parameter remained essentially unaltered. The distinct variations in the thoracic blood filling were probably dependent on the amount of blood shifted to the decompressed area which may be related not only to the venous capacity in this area but also to the venous-arterial reflexes and possibly to the specific transfer of reduced pressure in tissues.

[Text] The functional test with production of negative pressure to the lower half of the body (LBNP) was first used in spaceflight on the Salyut orbital station. After this, it began to be used in programs of periodic in-depth examination of orbital station crews during long-term missions. Vast material was obtained, from both ground-based studies and in weightlessness, concerning the nature of the reaction of the cardiovascular system to LBNP. The distinctions of regional circulation and redistribution of blood in organs and segments of the body have been studied considerably less. The mechanism of transmission of low pressure to deeper tissues, partial contribution to the response of superficial and deep-lying veins, and resistive vessels are also not entirely clear.

Our objective here included determination of dynamics of delivery of blood to different parts of the body (head, chest, abdomen, pelvis, lower extremities) as a function of LBNP level, as well as identification of the mechanisms of blood redistribution in response to this factor.

Methods

We conducted this study on 10 healthy male subjects 19-22 years of age (average height 175 cm, weight 73 kg). Six tests were performed with each subject, with production of -10, -20, -30, -40, -50 snd -60 mm Hg LBNP, each step lasting 3 min.

There were 1-2 day intervals between tests. To generate LBNP, we used a cylindrical vacuum chamber in which the subject was placed in recumbent position to the level of the superior tubercles of the iliac bones.

We used ^{59}Fe-labeled red blood cells to assess delivery of blood to different parts of the body. For this purpose, the radiopharmaceutical agent was injected intravenously, in the morning on a fasting stomach, in the form of sterile irone citrate solution in amounts of 0.2-0.3 μBq. After injection of the isotope, determination was made of radioactivity of the entire body in a low-background chamber with a gamma spectrometer, using four detectors that moved at uniform speed under the platform. A collimated detector placed over the tested region was used to measure radioactivity in different parts of the body and organs. The data were recorded on a multichannel amplitude analyzer. The tests began 14 days after injection of the isotope. By this time, incorporation of the tracer in erythrocytes reached 96.1±2.4% according to results of control readings of blood sample radioactivity.

Correlation and regression methods of analysis were used for mathematical processing of results.

Results and Discussion

The obtained data indicate that the volume of blood shifted from the upper to the lower half of the body depends appreciably on level of decompression, anatomical and physiological distinctions of different parts of the body (Figure 1). More than two-thirds of the changes are referable to LBNP in the range of -10 to -30 mm Hg. At such decompression levels, there was 23% less filling of vessels in the thorax, 19% less in the head and 23-26% more blood in the pelvic region and legs. With further reduction of LBNP to -40 and -60 mm Hg, only 13% of the blood shifted from the thoracic region, filling of the head region showed virtually no change, intensity of influx of blood to the legs constituted 14% and to the pelvis, 9%.

The abdominal region, where there were no statistically significant changes in delivery of blood, is a distinctive "neutral" point between segments with opposite directions of changes in blood volume (Figure 2). Analogous data were obtained by the authors of [12], who also failed to demonstrate changes in delivery of blood to the upper abdominal region at LBNP of -40 mm Hg. The existence of a "hydrostatically indifferent point" with use of postural factors [5] is confirmed, to some extent, by our data, the only difference being that its localization with LBNP is the same (in the region of the pressurization line), and may shift with change in position of the body.

Thus, efflux of blood to the lower half of the body occurs chiefly from the thorax, blood in which decreases by a mean of 36%. According to other

researchers [3], this decline constituted 18-27%. Since the low-pressure system plays the role of reservoir for blood, it can be assumed that the dynamics of delivery of blood to organs of the thorax are attributable to displacement of mainly venous blood. This is confirmed in studies of central venous pressure and pressure in the pulmonary artery with LBNP [2, 6, 13]. The same authors [2] report that maximum changes in the parameters in question already occur at low levels of exposure, attributing this phenomenon to the fact that low levels of diminished pressure are sufficient to stimulate low-pressure receptors, and that this distinction is due to change in capacity of veins in the region submitted to LBNP.

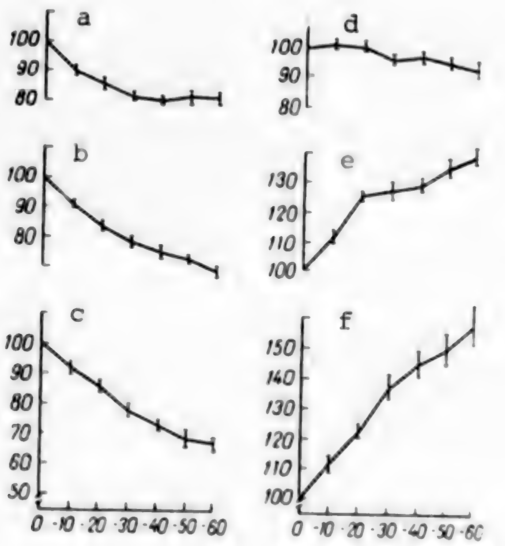

Figure 1.
Dynamics of flow of blood to body segments with LBNP
Here and in Figure 2: a-f refer to head, neck, chest, abdomen, pelvis and legs, respectively
X-axes, LBNP (mm Hg); y-axes, blood delivery, % of baseline level

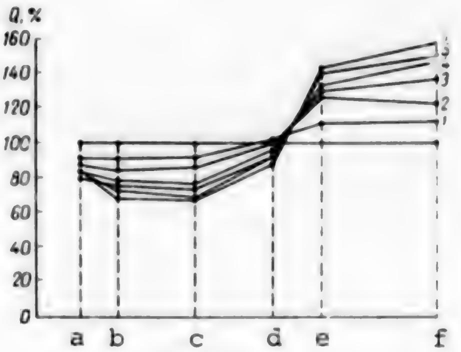

Figure 2.
Redistribution of blood in the body during LBNP
Y-axis, delivery of blood (%)
1-6) LBNP at -10, -20, -30, -40, -50 and -60 mm Hg, respectively

Indeed, this phenomenon could explain classical theses concerning dramatic increase in venous volume with insignificant elevation of transmural pressure due to passive change in vascular geometry. The data of R. S. Musgrave et al., P. B. Raven et al. [8, 9] could serve as confirmation of this; they observed that increment in leg volume is greater in individuals with varicose veins. Consequently, the amount of blood that can fit in the venous system of the legs or lower half of the body could determine the severity of changes in delivery of blood to the upper half of the body, in particular, thoracic organs.

Changes in blood filling of body segments in the decompression region are similar to those in the upper half of the body, but the extent varied. There was more significant (in some cases almost double) increase in delivery of blood to segments of the lower half of the body, as compared to the upper. There is probably a dual nature to redistribution of blood with LBNP. While a shift of interstitial fluid into the lumen of emptied vessels is observed in the upper half of the body [1] which partially replenishes the volume of blood in it, the reverse phenomenon occurs in the decompression zone: filtration of

plasma, shifting of fluid from the intravascular to the interstitial space and possible concentration of blood in vessels of the lower half of the body. According to V. C. Luft et al. [7], who measured total leg volume during LBNP, there is extravasation with possible formation of edema. However, as noted by P. B. Raven et al. [7], data from external measurement of limb volume are not sufficient to assess changes in intravascular volume.

The fact that the response of the circulatory system is virtually a proportionate function of LBNP level in the range of up to -20 to -30 mm Hg, which is observed by many authors, and change in its nature upon subsequent increase in this factor could also be attributable to physical processes in tissues that transmit low pressure. It should be borne in mind that 90% of the applied negative pressure is transmitted to a depth of only 2.5 cm [4]. The results of the studies of R. S. Musgrave et al. [8] indicate that much energy is expended on muscular extension, and for this reason transmural pressure is lower than expected. P. B. Raven et al. [9], who studied reactions of the cardiovascular system to LBNP in conditioned and unconditioned people, established that it may be difficult to interpret the data in view of the fact that not all levels of negative pressure are transmitted to vessels; one must take into consideration the constitutional distinctions and level of conditioning, since transmission of pressure may differ, depending on muscular development.

Local distension of vessels, including resistive ones, is the immediate effect of low pressure. While capacitive vessels begin to respond to low levels of the generated gradient of transmural pressure, resistive vessels probably become involved when the distending effect of transmural pressure reaches the threshold of sensibility of autoregulatory mechanisms, causing reflex vasoconstriction. Indeed, according to K. Skagen et al. [10, 11], vasoconstruction due to a local axon reflex develops at transmural vascular pressure of no more than 20-40 mm Hg. These authors [11], who studied circulation in the skin at low local pressure of -10 to -250 mm Hg, found that a marked vascular response appears when transmural pressure is increased from -20 to -40 mm Hg, and subsequent increase to -150 mm Hg is not associated with progressive changes.

Evidently, the absence of a marked dependence on intensity of the factor at high values of low pressure could be due to the fact that the initially set effect is curbed by triggering of a number of concomitant competing influences on vessels of the part of the body in the decompression zone. Such an integral parameter as filling with blood would, of course, reflect summation of these effects. It can be assumed that subcutaneous vessels are the chief site of deposition of blood, since the coefficient of transmission of negative pressure to deep tissues progressively diminishes. In order to comprehend the phenomena that occur in the decompression zone and determine the dynamics of blood filling as a function of magnitude of LBNP, it is necessary to examine simultaneously the changesin arteriolar and venous tone, and determine the coefficient of transmission of negative pressure to the vascular wall.

Thus, the dynamics of blood filling of the thoracic region, where reflexogenic zones are concentrated, will depend on the amount of blood redistributed to the zone of decompression which, in turn, may be due not only to capacity of veins in this zone, but triggering of venous-arterial reflexes, as well as the distinctions of transmission of negative pressure in tissues.

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HUMAN METABOLISM AND PERIPHERAL CIRCULATION DURING ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 1 Aug 86) pp 46-49

[Article by V. Ye. Vorobyev, I. V. Kovachevich, L. L. Stazhadze, V. F. Ivchenko, V. P. Abdrakhmanov, V. N. Kalyaneva, S. G. Voronina and L. G. Repenkova]

[English abstract from source] Metabolism and peripheral circulation were investigated in head-down tilt tests of varying duration. The greatest changes were seen on test day 30, when the subjects showed venous hyperoxia, lower oxygen arterio-venous difference and a significant ($p<0.05$) decrease of oxygen tension in arterial blood and oxygen utilization in tissues ($p<0.05$). At the same time the subjects exhibited an increase in Pi and lactate and a maximum growth of 2,3-diphosphoglyceric acid ($p<0.05$). This exposure seems to produce a discrepancy between oxygen supply and oxygen requirements in tissues which gives rise to secondary tissue hypoxia. It is believed that the basic cause of these changes is disordered oxygen transport from blood to tissues.

[Text] It was established in several studies that submitting man to antiorthostatic hypokinesia [head-down tilt] (HDT) elicits change in metabolic activity of tissues and changes in peripheral hemodynamics [2, 4, 5, 7, 8]. However, the nature and severity of these changes as related to increased duration of HDT have not been sufficiently investigated. Our objective here was to examine metabolic processes and peripheral circulation in subjects in a series of HDT tests of various duration.

Methods

We examined gas composition and metabolic component (BE) of acid-base equilibrium of venous blood, using ABL-2 equipment, in 32 essentially healthy men, in 4 series of studies involving 14- and 120-day HDT. Samples of arterial and venous blood were taken by puncture of the radial artery and ulnar vein without using a tourniquet. Blood oxygen content was calculated using the formula of Theye [11]. In addition, we calculated the arteriovenous difference for oxygen and percentage of tissular utilization of oxygen [1]. We assayed 2,3-diphosphoglyceric acid (2,3-DPG) in red cells isolated from the subjects' venous blood, using the method of N. P. Meshkova and N. V. Alexsakhina [6]. Concentration

Table 1. Dynamics of changes in metabolic parameters tested under effect of HDT (M±m)

Stage of study	Number of subj.	pO_2, mm Hg artery	pO_2, mm Hg vein	Vol.% O_2 artery	Vol.% O_2 vein	BE, mmol/ℓ	2,3-DPG, μmol/mℓ	IP, μmol/mℓ	O_2 utilization, %	AVD for O_2, vol%
Before HDT	19	96,1±1,4	34,5±1,0	15,1±0,2	5,7±0,3	−2,3±0,4	3,23±0,17	4,37±0,11	63,3±2,3	9,4±0,4
HDT day:										
3 (−8°)	11	87,7±2,9	25,0±1,1*	14,1±0,2	4,0±0,2**	−0,6±0,4	3,67±0,20	5,12±0,06	71,2±2,1	10,1±0,6
7 (−8°)	20	87,0±1,1**	25,1±1,1**	13,9±0,2*	4,0±0,2**	+0,4±0,3	3,49±0,11	4,75±0,10	71,2±1,4*	9,9±0,2
14 (−8°)	20	92,9±1,0	30,6±1,3	14,7±0,2	5,0±0,4	−2,2±0,3	3,54±0,12	4,68±0,09	65,8±1,2	9,7±0,4
30 (−4°)	12	86,2±2,7*	41,9±2,3*	13,8±0,3*	6,7±0,3	−3,3±0,6	4,15±0,24*	5,20±0,12**	51,8±2,7*	7,1±0,7*
55 (−4°)	12	85,3±3,2	29,6±3,8	14,5±0,3	5,8±0,7	−2,8±0,7	1,21±0,15**	5,35±0,21*	59,9±4,9	8,6±0,9
90 (−4°)	12	93,9±3,1	33,1±2,5	15,0±0,5	5,3±0,4	+0,1±0,3	1,38±0,17**	4,82±0,18*	64,9±1,8	9,7±0,2

Note: AVD--arteriovenous difference for oxygen content. *$p<0.05$, **$p<0.01$

of inorganic phosphate (IP) in venous blood plasma was determined by the method of Fiske and Subbarow [10], and lactate content was assayed using the Boehringer (FRG) kit. Concurrently, using a 4RG-1A rheograph and Galileo (Italy) encephalograph, we recorded rheograms of the finger by the conventional method [9]. We examined the following parameters: α/T, which reflects condition and elasticity of large and medium caliber arteries; dicrotic (DCI) and diastolic (DSI) indexes, which show tonus of arterioles and veins, respectively, parameter of intensity of pulsed blood flow (PBF) in vessels of the tested region. All studies were performed with the subjects at rest, in the baseline period in recumbent position and during HDT in antiorthostatic position. Reliability of differences, as compared to the baseline prior to HDT was assessed using Student's criterion.

Results and Discussion

Already in the first 2 weeks of HDT, the subjects showed noticeable decline of arterial blood oxygen tension, which was particularly marked on the 7th day (Table 1). However, this did not lead to a decrease in tissular oxygen uptake, since the subjects demonstrated reliable ($p<0.05$) increase in percentage of oxygen utilization and in arteriovenous difference for oxygen. In the same period, a statistically reliable ($p<0.05$) increase was demonstrated in blood filling of the finger, which could be due to attenuation of vasconstrictive influence of the vasomotor center (Table 2). However, the combined increase in tonus of arterial vessels (both precapillary and those of larger caliber) compels us to assume that the increasing plethora in this region is probably based on elevation of perfusion pressure, rather that decrease in peripheral vascular resistance.

Subsequent testing on the 30th day of HDT revealed insignificant decline, as compared to the 7th day, in oxygen tension of arterial blood. Nevertheless, this decline was associated with diminished

oxygen uptake by tissues. Evidently, the dissimilar capacity of tissues to utilize oxygen is the main cause of such a difference in tissular oxygen uptake response to lowering of pO_2 in arterial blood. Thus, while on the 7th day of HDT tissular utilization of oxygen in the subjects occurred rather intensively, as indicated by reliable decline ($p<0.01$) decline of its tension in venous blood, the venous hyperoxia demonstrated on the 30th day of HDT is indicative of worsening of this capacity (see Table 1).

On the 55th and particularly 90th days of HDT, the subjects showed gradual improvement (as compared to the preceding stage of the study) in oxygenation of tissues. This is confirmed by the tendency toward increase in percentage of oxygen utilization and in arteriovenous difference (AVD) for oxygen, which are related to fuller extraction of oxygen from venous blood.

Table 2. Dynamics of parameters of finger rheograms

Parameter	Baseline	Day of HDT			
		3	10	30	49
RI, relative units	1,78±0,22	3,11±0,64*	3,39±0,84*	2,40±0,14	1,98±0,25
DCI, %	51,71+5,86	56,11±6,69	49,41±6,67	52,31±5,75	48,73±7,21
DSI, %	63,92+5,39	63,79±8,36	56,41±5,52	58,31±6,43	56,39±6,93
α/T, %	11,02±0,76	13,65±1,91	11,21±1,73	10,90±2,32	12,42±1,46

* $p<0.05$. RI--rheographic index [?]

The question arises as to whether the decline of oxidative processes, which occurred in the subjects by the 30th day of HDT, can be interpreted as the result of impaired tissular utilization of oxygen, or whether it is attributable to changes in delivery of oxygen to tissues.

In examining this questioı let us call attention to the following. In the first place, a reliable ($p<0.05$) decrease in oxygen content of arterial blood was demonstrated on the 30th day of HDT (see Table 1), which is considered one of the factors leading to diminished rate and intensity of delivery of oxygen to tissues [3]. In the second place, it is expressly in this period that maximum increase in IP was demonstrated in blood, as well as increase in concentration of lactate (to 0.73±0.09 mmol/ℓ, versus 0.45±0.07 mmol/ℓ in the baseline period before HDT). In the third place, at this same time, erythrocytes showed maximum concentration of 2,3-DPG (see Table 1), on the level of which the oxygen-transport function of blood depends.

A comparison of these figures leads us to assume that poorer deliverv of oxygen to tissues of subjects submitted to HDT leads to the following phenomena: shift of tissular metabolism, which is manifested the most adequately by processes occuring in the form of increase in levels of anaerobic metabolits--lactate and IP; compensatory increase in 2,3-DPG level in red blood cells, which accelerates oxygen transport to tissues.

Nor can we rule out the possibility that impairment of regional blood flow plays a substantial part in impairing regional blood flow. However, as shown by the results of these studies, an increase in duration of HDT did not have a noticeable

effect on intensity of delivery of blood to the finger and, consequently, to change in peripheral blood flow. At any rate, this cannot be construed as the principal factor making oxygen transport to tissue difficult, and it serves as definite evidence of the fact that impairment of oxygen transport from blood to tissue is the main element in changing delivery of oxygen to tissues of subjects subjitted to HDT.

All of the foregoing warrants the belief that decline of the level of oxidative processes occurring in subjects during HDT is attributable not only to decrease in tissular oxygen requirement due to restricted motor activity, but perhaps also inconsistency between tissue oxygen requirement and delivery. This can be confirmed by development of signs of metabolic acidosis in the subjects, and it was the most marked on the 30th day of HDT. Base deficit (BE) increased to -3.3 ± 0.58 mmol/ℓ (versus -2.3 ± 0.41 mmol/ℓ in the baseline period before HDT).

Thus, as a result of this study it was established that HDT conditions are characterized by inconsistency between delivery of oxygen and oxygen requirements of tissues, which leads to development of secondary tissue hypoxia.

Worsening of tissue's capacity to extract oxygen from blood is probably also rather important. Perhaps this is due to the fact that, under hypoxic conditions, there is less affinity of the polyenzyme system of mitochondria to oxygen [3]. Analysis of data on change in concentration of 2,3-DPG, which were obtained on the 30th day of HDT, indicates that there is diminished affinity of hemoglobin for oxygen, and this can apparently be viewed as indirect evidence of diminished affinity of tissues for oxygen. At the same time, since the body starts to adapt to a shortage of oxygen (judging from the results of tests on the 55th and 90th days of HDT), we cannot rule out hypokinesia in this period and biochemical adaptation--increased arfinity of tissues for oxygen.

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577.175.522]-06:612.766.2

DISTINCTIONS AND MECHANISMS OF EFFECTS OF EPINEPHRINE AND NOREPINEPHRINE ON CARDIAC PUMPING FUNCTION UNDER HYPOKINETIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 16 Mar 86) pp 49-52

[Article by A. S. Chinkin]

[English abstract from source] The effect of epinephrine (E) and norepinephrine (NE) on cardiac output (CO) and heart rate (HR) of hypokinetic and control rats was studied. It was found that in the hypokinetic animals the E effect on CO was significantly weaker than in the controls while the NE effect was stronger. In most experiments the response to NE in the hypokinetic animals was greater than that to E. The mean HR increase was not significantly different in the two groups but in the hypokinetic rats the response to E was less expressed. These data give reason to believe that the lower E effect on CO in the hypokinetic animals is associated with diminished α-adrenergic effects on the heart.

[Text] It was previously shown that the effect of epinephrine (E) on parameters of cardiac contractile function is attenuated under hypokinetic conditions, while the effect of norepinephrine (NE), on the contrary, is more effective than in the control [7]. However, no studies were made of the mechanisms of the changes in different directions in inotropic effects of these catecholamines (CA) under hypokinetic conditions. Due to absence of direct data, the extent to which these distinctions of E and NE effects are relevant to stroke volume (SV) of blood, which is related not only to myocardial contractility but possible influence of CA on resistive and capacitive vessels, is not quite clear [1-10].

This prompted us to undertake the present study, the purpose of which was to examine the distinctions of E and NE effects on pumping function of the heart during hypokinesia, with analysis of their effects in the case of selective and combined blocking of β- and α-adrenoreceptors (AR).

Methods

Male albino rats were divided into two groups. The 1st, control group (13 animals) was kept in ordinary cages at a temperature of 15-20°C. The animals

of the 2d group (9 rats) were kept in individual box-cages, which limited their motor activity, for 22-23 h/day for 30 days, in order to produce hypokinesia. To attenuate the stress reaction inherent in hypokinesia [2], these animals were moved for 1-2 h per day to a common [larger] cage, and the stay in the confined cages was increased gradually for 15 days prior to the basic experiment.

Upon conclusion of the hypokinetic period, the animals of both groups were anesthetized with urethane (1.25 g/kg) and, to rule out development of baroreflex bradycardia via the vagus nerves, we gave them atropine (1.5 mg/kg). SV was measured by tetrapolar transthoracic impedance rheography. To record the differential rheogram, needle electrodes were applied subcutaneously: exploring ones on the level of attachment of the clavicle to the sternum and xiphoid process, and active ones, to the lower lip and right thigh. Rheograms were recorded using an RPG-204 instrument and N-338 recorder at paper feeding rate of 100 mm/s at the following times: before and 10 min after giving atropine, before and for 40 s after successive (at 10-12 min interval) administration of E and NE (1 μg/kg each intravenously in a volume of 0.5 mℓ/kg isotonic solution of NaCl), before and 8-10 min after hypodermic injection of obsidan (5 mg/kg), repeated administration of the same dose of E after obsidan, before and 5 min after intravenous injection of phentolamine (5 mg/kg) and another injection of E after this.

SV was calculated using the formula of W. G. Kubicek et al. [11], considering that specific resistance of blood is 150 Ω/cm. Heart rate (HR) was also determined from the rheogram. Maximum effects of CA (as a rule 10-15 s after administration) were expressed as percentage of baseline SV and HR obtained just prior to administration.

In addition to the basic series of experiments, we conducted preliminary studies on control animals, in which we either changed the order of blocking α- and β-AR or the dosage of CA under completely identical experimental conditions. Some of the data from these studies will be used in discussing the results of the main series.

Results and Discussion

By the end of the hypokinetic period, the weight of animals in the experimental group constituted a mean of 298±8.0 g, which is reliable ($p<0.01$) lower than for control animals (384.4±10.2 g). However, this difference (~10%) is relatively small, and this is perhaps related to the less stressogenic effect of intermittent hypokinesia that we used. HR of experimental group animals was significantly higher and SV lower than in the control; thus, cardiac output was essentially the same ($p>0.5$) in both groups of rats. After giving atropine, SV dropped reliably in control animals, apparently due to significant (by 29.4±5.7%, $p<0.001$) increase in HR. The effects of atropine, particularly the chronotropic effect, were not marked in hypokinetic animals, and this confirms data in the literature concerning attenuation of vagal-cholinergic influences on the heart as a result of hypokinesia [2, 5].

Mean increment of HR did not differ reliable in the two groups under the effect of E and NE, but there was a tendency toward less marked effect of E during hypokinesia. As for SV, the effect of E on hypokinetic animals was lower by

a factor of 2.5 ($p<0.01$) than in controls, while the reaction to NE was somewhat greater and, unlike the control, exceeded the response to E in most tests. Consequently, the correlation between systolic effects of E and NE during hypokinesia is analogous to the correlation between their inotropic effects [7].

After blocking β-AR with obsidan, as was to be expected HR decreased in both groups ($p<0.001$), while SV increaskd, which is also consistent with the literature [13]. The chronotropic effect of obsidan was somewhat greater in hypokinetic animals, while the increment of SV was 2.5 times greater in the control ($p<0.05$), which is indicative of substantial differences in mechanisms of regulation of these two parameters, which determine cardiac output. Indeed, as was shown previously [8] and, with respect to E, in this study, while loss of β-adrenergic influences on the pacemaker could hardly be replaced by activation of other adrenergic mechanisms, a β-AR block signifies for SV the loss of only the positive effect of NE. The positive effect of E in this case, is not only retained, but even enhanced in a number of instances, as was observed in hypokinetic animals. A significant potentiation of the systolic effect of E after β-blocking was also demonstrated in control animals and those adapted to a physical load [8]. However, in our study, control animals showed attenuation of the effect, which is nevertheless unexplainable and will be discussed below.

It is apparent from the above data that the positive effect of NE on SV is a β-adrenergic response. After selectively blocking α-AR, as shown by preliminary experiments, it did not change (22.5±6.8%, versus 23.1±3.2% before the block). The effect of E, however, weakens (from 31.2±4.2 to 23.6±4.6%) although unreliably ($p>0.05$). In the case of a combined block of α- and β-AR, there was significant decrease in positive of effect of E on SV, and it was demonstrable in only some of the experiments in both groups; in others there was no effect or else it was even negative. Consequently, this E effect occurs through both types of AR, α and β. As shown by studies of isolated preparations of different parts of the heart, an analogous route is inherent in the inotropic effect of E, whereas NE activate, here too, only β-AR [14]. Such a coincidence of distinctions of expression of systolic and inotropic effects of CA suggests that their effect on SV was obtained in our experiments mainly through α- and β-AR, and that analogous receptors of smooth muscle cells of vessels did not play any appreciable role here. Indeed, whey did NE fail to increase SV after the β-block by, let us say, affecting α-AR of capacitive vessels, thereby stimulating venous return? Or why did the α-AR block fail to influence the systolic effect of NE, in spite of the fact that, in this case, it would seem that the vessels were deprived of the vasoconstrictive influence of amine? Perhaps it is only a matter of stimulation of AR of both capacitive and resistive vessels by exogenous CA, which are not strictly addressed, as a result of which their influence of SV is in different directions and, to a significant extent, mutually compensated. The fact that CA have virtually the same effect on both capacitive and resistive vessels is in favor of this assumption [12].

Consequently, the aggregate of above data (some increase in negative effect of obsidan on HR, as well as positive effect of NE on HR, SV and myocardial contractility [7]) warrants the belief that β-adrenergic influences on the heart increase as a result of hypokinesia.

Conversely, as a result of prolonged hypokinesia cardiac α-AR activity diminishes, and attenuation of the E effect on SV could be largely related to this change. It has been shown [9] that there is an extremely mild SV response, as compared to the control, during hypokinesia and in response to the α-adrenoagonist, mezaton (neo-synephrine], and its effect, like E, is potentiated by obsidan. However, it was found that this is not the specific effect of hypokinesia, but rather the result of the special interactions between obsidan and mezaton, where the mild effects of the latter, regardless of whether the animal was in the hypokinetic or control group, was enhanced by obsiden, while marked effects were, on the contrary, depressed. Analogous interaction with obsidan is inherent in E. It was previously established [8] that mild effects (mean 5.8±2.2%) of lower doses of E (0.5 μg/kg) following a block of β-AR showed almost a 4-fold increase ($p<0.001$) in control animals, whereas the more marked effects of E in the control group in our study were generally attenuated. However, when we submitted the value of the E effect on these animals before and after giving obsidan to correlation analysis, the coefficient was rather high with a negative sign, 0.878. Consequently, only marked effects were also attenuated in the control group, whereas relatively mild ones were enhanced. Aggregate analysis of data referable to control and hypokinetic animals also yielded a high coefficient ($r = -0.740$).

The submitted data indicate that the dual interaction with obsidan is possibly inherent in all α-adrenoagonists of the myocardium. On the one hand, this confirms a hypothesis we expounded [8, 9] concerning the possible involvement of obsidan in activation of myocardial α-AR, and on the other hand it is indicative of a link between the mild effect of E on SV during hypokinesia and low activity of α-AR. However, the question arises as to why, in the absence of adrenoblocking agents, E does not have a significant effect on SV of hypokinetic animals via myoacardial α-AR, the activity of which is rather high in the experimental group, according to the reaction to NE. This is probably attributable to the fact that, as a result of hypokinesia, myocardial β-AR reactivity to E diminishes and to NE it increases which, in turn, could be due to the increase in myocardial concentration of E and decline of NE level that are inherent in hypokinesia [6]. Evidently, the change in correlation and chronotropic effects of these amines in hypokinetic animals speaks in favor of such a hypothesis.

In conclusion, let us note that, against the background of obsidan action, administration of phentolamine lowered HR by a mean of 10% in both groups. This is apparently indicative of the fact that, in the absence of β-adrenergic influences, HR can be controlled via α-AR. SV also decreases under the influence of phentolamine, but the effect is reliable only in the control group of animals ($p<0.01$). Under hypokinetic conditions, the decline is less significant, and it is not observed in all experiments, which is apparently indicative of attenuation of the role of α-AR in implementing the effects of endogenous catecholamines on SV.

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BIORHYTHMOLOGICAL ANALYSIS OF DYNAMICS OF PULMONARY VENTILATION PARAMETERS DURING ORTHOSTATIC TESTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 3 Oct 86) pp 52-59

[Article by V. A. Galichiy]

[English abstract from source] Pulmonary ventilation parameters (breathing depth, frequency and minute volume, and alveolar ventilation) of 5 healthy male test subjects who performed a 20-minute tilt test were analyzed. During tilt tests the above parameters showed oscillations in a range of about 1 minute. During the first 1-3 minutes of exposure the parameters exhibited an accentuated synchronization of the oscillations and the phenomenon of "general autonomic switch-over" with the negative phase (fall of the parameters under study below the baseline level after an initial increase above the baseline level). From the 4th minute till the 6.5th minute the function of individual components of the pulmonary ventilation system mismatched and the respiration efficacy fell. Thereafter this synchronization of the processes studied returned to the normal. Adequate adaptation of pulmonary ventilation to tilting developed not earlier than during the 13-14th minute.

[Text] It is known that oscillatory processes in the body, biological rhythms, are adaptive and serve to maintain homeostasis [1, 2, 4, 5, 8, 12]. There are grounds to believe that the body's reactions to stressors also occur in an oscillatory mode [13], whereas the dynamics of these reactions demonstrate periods of "functional wellbeing" and "functional adversity." Demonstration of these periods is important to diagnosis of functional state and prognosis of tolerance to stress factors. The biorhythmological approach to analysis of material permits detection of these periods.

We did not encounter, in the accessible literature, any works dealing with the biorhythmological distinctions of responses of the external respiratory system to orthostatic factors. This is why the present investigation was undertaken.

Methods

We are submitting the results of testing 5 healthy men 26 to 40 years of age, who performed a passive 20-min orthostatic test in the morning, on a fasting stomach. We used a turntable to switch the subject in 3 s from horizontal to head-up position with body tilted 70° from the horizontal plane. External respiratory function was evaluated for 10 min in the baseline supine position and for 20 min during the orthostatic test. Using a Beckman MMC metabolimeter, operating on the Exercise program, we recorded minute volume ($\dot{V}_E$), tidal volume (V_T), respiratory rate (f) and minute volume of exhaled carbon dioxide ($\dot{V}_{CO_2}$). Fractional concentration of carbon dioxide in alveolar air ($F_{A_{CO_2}}$) was measured with an additional Beckman LB-2 carbon dioxide gas analyzer, the readings of which were recorded in the form of a capnogram on a Beckman RR-2 automatic recorder. Parameters $\dot{V}_{CO_2}$ and $F_{A_{CO_2}}$ were used to calculate alveolar ventilation with the following formula:

$$\dot{V}_A = \frac{\dot{V}_{CO_2} \cdot 100}{F_{A_{CO_2}}}$$

The MMC metabolimeter was operated in an automatic averaging mode during measurement of a whole number of respiratory cycles at a set interval (breath cycle operating mode).* For the first 8 min of the baseline period, averaging was made for every 2 min, and in the next period (including the entire 20 min of the orthostatic test), every 30 s.

The analyzed parameters were expressed as percentage of baseline, which was expressed as the arithmetic mean of all values recorded prior to the test. The data obtained on all subjects were averaged. As a result, we obtained a numerical series of 30 values for each functional parameter, and they were plotted on a graph.

Since the dynamics of analyzed parameters demonstrated in their graphic expression an oscillatory process, we submitted to analysis the amplitude and frequency characteristics of these oscillations. The period of each oscillation was measured by the distance between two adjacent minimums and the amplitude, by the difference between maximum and minimum of each wave. Since all points on the plots were expressed as percentage of baseline level, the difference between them (amplitude) was also presented as a percentage. This scale had no independent meaning, but it enabled us to compare the amplitudes of different functional parameters.

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*This was afforded by the fact that the actual interval in which respiratory cycles were counted could exceed the given length by as many seconds as needed to complete the last cycle. Scaling per minute was made by the MMS computer with a margin of error of tenths of a respiratory cycle.

Thus, the respiration rate was measured without error. Margin of error in determining other parameters constituted ±4% for $\dot{V}_E$, $\dot{V}_{CO_2}$, V_T, and ±2% for $F_{A_{CO_2}}$.

In addition to amplitude and period, we assessed the level of each wave--the half-sum of maximum and minimum. The dynamics of digital values of amplitude and level were also rendered graphically (their plotting on the time scale was arbitrarily coordinated with the peaks of corresponding waves).

The analyze the closeness of relationship between parameters studied, we examined the correlation between them at different stages of the orthostatic test. The coefficients of correlation were calculated by the conventional method and checked for statistical reliability [7].

In addition, we determined one of the criteria of efficiency of external respiration, the ratio of alveolar ventilation to minute volume. The dynamics of this parameter were rendered in averaged form for values referable to five subjects.

Results and Discussion

All of the parameters studied fluctuated within the range of about 1 min during the orthostatic test (Figure 1, Table 1). Four periods were distinctly demonstrable to the dynamics of depth of respiration. The first (1st-3d min of orthostatic test) was characterized by frequent high-amplitude oscillations, the second (4th to start of 7th min) included one elongated low-amplitude wave), the third (7th-13th min) represented another group of frequent high-amplitude waves and the fourth (14th-20th min) included a second elongated low-amplitude wave followed by a half-wave of equally smooth amplitude. Consequently, depth of respiration during the orthostatic test was characterized by alternation of more frequent high-amplitude and less frequent low-amplitude oscillations.

Table 1. Period and amplitude of fluctuation of parameters of pulmonary ventilation during 20-min passive orthostatic test

Parameter of pulmonary ventilation	Duration of period, min		Amplitude, %
	range of variation	arithmetic mean	
Minute respiratory volume ($\dot{V}_E$)	1,0-3,5	1,8	18±2,0
Alveolar ventilation ($\dot{V}_A$)	1,0—4,5	2,9	25±1,6
Depth of respiration (V_T)	1,0—2,0 —	1,5 2,5*	26±2,6 11
Respiration rate (f)	1,0—2,5 3,0—5,0	1,5 3,6	14±1,2 23±1,5

Note: Data referable to 5 subjects are listed.
*Indicates 2 waves with identical period and amplitude.

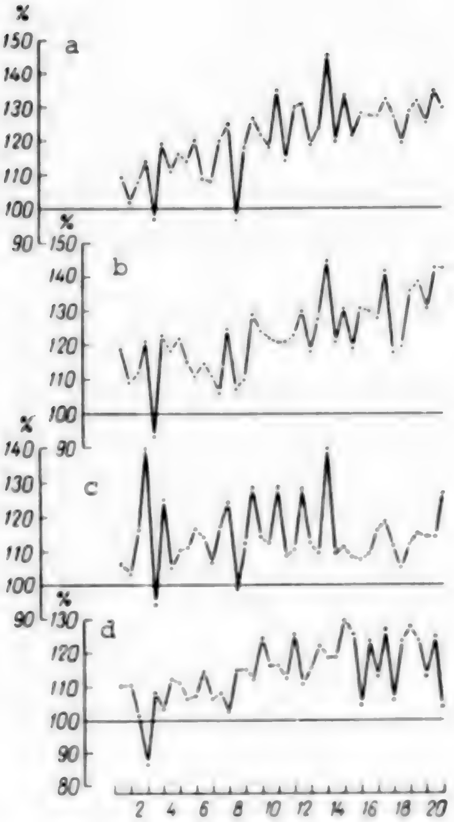

Figure 1.

Dynamics of parameters of pulmonary ventilation during passive orthotest (% of baseline values)
Here and in Figure 2: x-axis, min of orthostatic test; y-axis, a, b, c, d--$\dot{V}_E$, $\dot{V}_A$, V_T and f, respectively (%)

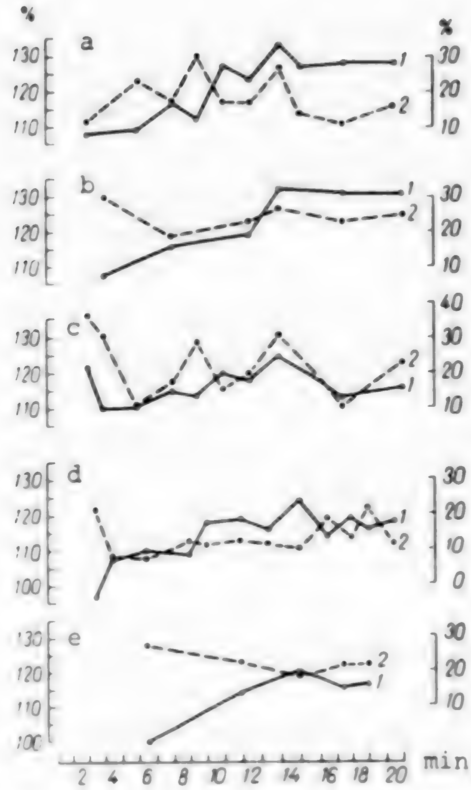

Figure 2.

Dynamics of level (1) and amplitude (2) of fluctuation of parameters of pulmonary ventilation during passive orthostatic test
Y-axis, left--level of oscillations (%): right, amplitude of oscillations (%); a, b, c, d, e--$\dot{V}_E$, $\dot{V}_A$, V_T, f (τ= 1.5 min) and f (τ= 3.6 min), respectively

Oscillations with greater and smaller periods were also demonstrable in dynamics of respiration rate, but the nature of correlation between them was different: smaller waves were superimposed here on larger ones. These large waves could be distinguished on the curve on the basis of minimal values for the parameter (see Figure 1, Table 1).

Evaluation of dynamics of levels of tested parameters merits special attention. Figure 1 shows that, within the first 3 min of the orthostatic test, there are two opposite phases: elevation above baseline (positive phase) followed by brief decline below the baseline (negative phase). The negative phase was found to be the most marked in dynamics of respiration rate and least noticeable in the dynamics of minute volume. On the average, for all recorded parameters, the depth of the negative phase was characterized by a drop to 7% below the baseline.

The negative phase is a fragment of a two-phase response known in the literature as the phenomenon of "general autonomic switchover" [14]. It consists in essence of alternate dominance of sympathetic and parasympathetic tonus in the general autonomic balance (i.e., in alternation of sympathotonic and parasympathotonic phases). The opinion is held that such undulant (and polyphasic, rather than merely biphasic) nature of reactions is a consistent sign of adaptation to the most varied stress factors [13].

Facts have been described in the literature indicative of a negative phase during orthostatic tests also. There was indication of the dynamics of some parameters of external respiration, but these data were not submitted to purposeful analysis [6, 9]

It can be assumed that the oscillations of parameters of pulmonary ventilation above and below the baseline level, which we observed at the early stage of the orthostatic test, are also a reflection of alternation of sympathotonic and parasympathotonic phases, which should be evaluated as a normal manifestation of adaptive reactions of the system of external respiration to an orthostatic factor.

In assessing human reactions to orthostatic factors, emphasis is usually laid on the sympathotonic nature of these responses [10]. The data from the present study indicate that sympathotonic effects may be followed for some time by the opposite, parasympatotonic effects at the early stage of the orthostatic test (first 3 min). And, if we consider individual constitutional distinctions, we can assume that the time of autonomic switchover, as well as depth and duration of the negative phase will differ in each instance.

For this reason, when determining orthostatic stability of man, it is necessary to consider in each concrete case both the time of change in phases and the extent of their expression. We cannot rule out the possibility that excessive expression and duration of vagotonic reactions (i.e., the negative phase) may be adverse signs indicative of diminished human tolerance to the orthostatic factor. This question is of practical importance and requires further investigation.

Starting with the 4th min of the orthostatic test, we observed a second rise of the parameters under study above the baseline level. The values for alveolar ventilation and respiratory rate held at a high level to the end of the study, while minute volume and depth of respiration were again below the baseline in the 8th min of the orthostatic test. This decline, however, was brief and insignificant (second, mild negative phase). Thereafter, the parameters again rose and held at above the baseline level (see Figure 1).

Thus, the inherent distinction of dynamics of pulmonary ventilation during the orthostatic test was fluctuation of values of the tested parameters. With the exception of brief (but important in its physiological implication) negative phases, the levels were above the baseline, which is indicative of the leading role of sympathotonic reactions as compared to vagotonic ones during the orthostatic test.

If we were to express the level as the half-sum of maximum and minimum recorded within each wave and submit these data graphically (Figure 2), we shall find that, starting in about the 4th min of the test, it gradually rose. This rise was not uniform (in steps in a number of cases) and ended with achievement of maximum values by the 13th-14th min. Thereafter, minute volume, alveolar ventilation and respiratory rate held at close to the maximum level, whereas depth of respiration diminished significantly and remained low to the end of the study.

Consequently, the period from the 1st to the 13th-14th min of the orthostatic test was notable for marked instability of the parameters studied. This warrants the assumption that satisfactory adaptation of the system of pulmonary ventilation to passive orthostatic tests is obtained on the average no sooner than the 13th-14th min, and only the subsequent period can be characterized as one of relatively stable functioning.

As for the amplitude of the analyzed fluctuations, it was difficult to detect any patterns in common to all four parameters in its dynamics. In this respect, the greatest similarity was noted for parameters of minute volume and depth of respiration, the dynamics of amplitude of which were characterized by the presence of two peaks (see Figure 2). It is only at the early stage of the orthostatic test that we could single out a distinction in common to all analyzed parameters: increase in amplitude, which was the most marked in parameters of depth of respiration and alveolar ventilation.

The correlations between the studied parameters were analyzed as related to the orthostatic factor as a whole, as well as its different stages, with special reference to periods that were singled out in analysis of the dynamics of tidal volume and, in addition, the period from the 1st to 13th min, which was characterized by particular instability of levels (Tables 2-4). First of all, we were impressed by the fact that there was a particularly close correlation between minute volume, on the one hand, and alveolar ventilation and tidal volume, on the other, as well as very marked negative correlation between depth and rate of respiration in the first 3 min of the orthostatic test (see Tables 2-3). The second period of the orthostatic test (from the 4th to middle of the 7th min) was characterized by impairment or attenuation of these correlations, as manifested by change in sign of the coefficient of correlation, decrease in its value with concurrent loss of statistical reliability. In the next two periods (middle of the 7th-13th and 14th-20th min) we were able to observe either restoration of relationship inherent in the first period, or a tendency toward recovery without achievement of the initial close relationship.

The very marked correlation between the parameters studied in the first 3 min of the orthostatic test actually signifies a high degree of synchronization of activity of different elements of the external respiratory system. It was established that intensification of reciprocal synchronization of rhythmic processes in the body is often observed under stress regardless of its concrete nature [13]. According to the principle of "alternating activity of functional structures" of G. N. Kryzhanovskiy [11], at relative rest the entire reserve of functional capacities of an organ or system is never realized immediately: there is alternate involvement of some structures, then others or groups of structures, thereby providing for the optimum correlation between phases. Such asynchronous activity is an important prerequisite for prompt and complete

recovery of functional strcutures after the period of their activity. However, if it is necessary to maintain a high level of functional activity of an organ or system, the number of simultaneously functioning entities increases, i.e., there is increase in number of synchronously functioning structures. Such activation of reserves is indicative of a particularly stressed functional rhythm of an organ or system.

Table 2. Coefficients of mutual correlation between depth and rate of respiration, as well as minute volume and alveolar ventilation at different stages of orthostatic test

Period of orthostatic test, min	Depth and frequency of respiration			$\dot{V}_E$ and $\dot{V}_A$		
	r	quality of relationship	statistical reliability of correlation coefficient	r	quality of relationship	statistical reliability of correlation coefficient
1st–3d	−0,895*	Close	$0,01<p<0,02$	+0,926*	Close	$p<0,01$
4th–first half of 7th	−0,130	None	—	−0,317	Moderate	$p>0,1$
Second half of 7th–13th	−0,344	Moderate	$p>0,1$	+0,833*	Close	$p<0,01$
1st–13th	−0,303	Moderate	$p>0,1$	+0,906*	Close	$p<0,01$
14th–20th	−0,295	Minimal	$p>0,1$	+0,816*	Close	$p<0,01$
Overall	−0,298	Minimal	$0,05<p<0,1$	+0,816*	Close	$p<0,01$

*Statistically significant correlation, here and in Tables 3 and 4.

Table 3. Coefficients of correlation between depth of respiration [tidal volume] and parameters of minute volume and alveolar ventilation at different stages of orthostatic test

Period of orthostatic test, min	V_T and MV			V_T and $\dot{V}_A$		
	r	quality of relation ship	statistic. reliability of correlation coefficient	r	quality of relation ship	statistic. reliability of correlation coefficient
1st-3d	+0,840*	Close	$0,02<p<0,05$	+0,651	Apprec.	$p>0,1$
4th-first half of 7th	+0,698	Appreciable	$0,05<p<0,1$	−0,524	Apprec.	$p>0,1$
Second half of 7th-13th	+0,865*	Close	$p<0,01$	+0,964*	Close	$p<0,01$
1st-13th	+0,710*	Close	$p<0,01$	+0,683*	Apprec.	$p<0,01$
14th-20th	+0,551*	Apprec.	$0,02<p<0,05$	+0,705*	Close	$p<0,01$
Overall	+0,545*	Apprec.	$p<0,01$	+0,484*	Moderate	$p<0,01$

Table 4. Coefficients of correlation between respiratory rate and parameters of minute volume and alveolar ventilation at different stages of orthostatic test

Period of orthostatic test, min	Respir. rate and MV			Respiratory rate and $\dot{V}_A$		
	r	quality of relationship	statistical reliability of correlation coefficient	r	quality of relationship	statistical reliability of correlation coefficient
1st-3d	−0,530	Apprec.	$p>0,1$	−0,434	Moderate	$p>0,1$
4th-first half of 7th	−0,371	Moderate	$p>0,1$	+0,596	Apprec.	$p>0,1$
Second half of 7th-13th	+0,107	None	—	+0,043	None	—
1st-13th	+0,322	Moderate	$p>0,1$	+0,162	None	—
14th-20th	+0,113	None	—	+0,112	None	—
Overall	+0,385*	Moderate	$0,01<p<0,02$	+0,351*	Moderate	$0,02<p<0,05$

It is known that the human cardiorespiratory system starts to function in a more strained mode when moving from horizontal to erect position. The same is indirectly indicated by the fact that the physiological effects of the test with lower body negative pressure are similar in many respects to the effects of the passive orthostatic test [3], which are characterized by some authors as "powerful stress" [15].

The foregoing warrants the belief that the particularly distinct mutual synchronization of tested parameters, which was demonstrated in the first 3 min of the orthostatic test, is the direct result of mobilization of the external respiratory system in response to the rapid change from horizontal to erect position, one of the emergency mechanisms of adaptation of this system to an orthostatic factor.

The second period of the orthostatic test (from the 4th to middle of the 7th min), with its typical attenuation or distortion of correlation between tested parameters, i.e., impairment of their synchronism, coordination, merits special attention. It could have been called the "period of discoordination" (or "period of mismatch") of the different elements of the system of external respiration. Judging from the ratio of alveolar ventilation to minute volume, it can be assumed that efficiency of external respiration progressively diminished in this period. At the time of maximum decline (middle of the 7th min), it was substantially lower than the baseline (Figure 3). All this indicates that the period from the 4th to middle of the 7th min of the passive orthostatic test was characterized by signs of functional impairment of the pulmonary ventilation system.

We cannot rule out the possibility that during the "mismatch period" there is an increased probability of development of orthostatic collapse, so that no additional burdens should be imposed in this period.

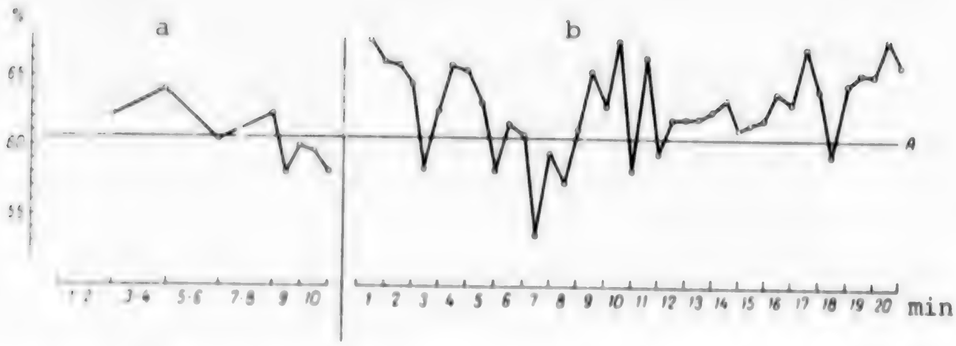

Figure 3. Ratio of alveolar ventilation to minute volume ($\dot{V}_A/\dot{V}_E$) before (a) and during (b) passive orthostatic test

A) arithmetic mean of baseline values

It must be stressed that we succeeded in detecting the "mismatch period" only through stage-by-stage correlation analysis, which was performed for relatively short intervals (3-7 min). If however, such analysis is made for the 13th or 20th min of the orthostatic test, the "discoordination period" remains hidden (see Tables 2 and 3). Thanks to step-by-step analysis, it was also possible to distinctly demonstrate the fact that the parameters of minute volume and alveolar ventilation were more closely related to tidal volume than to rate. This is apparently indicative of the leading role of depth of respiration in the mechanism of maintaining pulmonary ventilation during exposure to orthostatic factors.

Thus, we succeeded in establishing, using the biorhythmological approach to analysis of obtained data, that the dynamics of parameters of pulmonary ventilation during the period of orthostatic testing were represented by fluctuations in a range of about 1 min. Physiologically heterogeneous periods were found. The initial period (1st-3d min) was noted for mobilization of external respiratory function in response to change from horizontal to erect position. Marked syncrhonization of different parameters was the external expression of such mobilization. Another distinction of the first period was the negative phase, manifestation of "general autonomic switchover," which consisted of alternate prevalence of sympathetic and parasympathetic tonus in the body's autonomic balance. The period from the 4th to middle of the 7th min of the orthostatic test was characterized by desynchronization of different functional elements of the pulmonary ventilation system, associated with signs of diminished efficiency of respiration, so that this period could be assessed as a "functionally adverse" period and we can note that it is undesirable to use any additional factors at this time.

Thereafter, there was restoration of mutual synchronization of the tested parameters. The distinctive features of this recovery warrant the belief that satisfactory adaptation of the system of pulmonary ventilation to conditions of passive orthostatic tests is reached on the average no sooner than the 13th-14th min.

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NYSTAGMOMETRIC DISTINCTIONS OF INDIVIDUALS REGULARLY EXPOSED TO VIBRATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 1 Aug 86) pp 59-62

[Article by T. A. Nalimova]

[English abstract from source] Workers regularly exposed to vibration whose work record was not less than 10 years were examined. Nystagmometric data derived from caloric and optokinetic tests performed before and after work shifts were analyzed. The amount of atypical reactions was the greatest in the caloric and optokinetic tests carried out before work shifts. This was suggestive of the trend toward normalization discerned in the "afternoon reactions." The phenomenon of normalization can be added to the list of objective symptoms that are typical of vibration sickness.

[Text] Vestibular changes in individuals engaged in occupations involving exposure to vibration are attracting the close scrutiny of researchers [1-3, 9-12, 14]. A special aspect of the problem is referable to changes that take place in the course of a work day. That such changes exist is indicated by nystagmometric data obtained in rotation tests on the same individuals before and after a work shift [10, 14]. Our objective here was to compare nystagmometric data from caloric and optiiinetic tests at different times of day (before and after work) among workers in professions where exposure to vibration is involved.

Methods

We studied 12 people (sanders, fettlers, wreckers) with work tenure of 10 or more years during exposure to local vibration at a frequency of 16-1000 Hz, generated by a vibrating tool.

Each worker was tested twice, before work ("morning" reactions) and after the end of the work shift ("evening" reactions) using the classical bithermal test of Hallpike. We recorded 96 electronystagmograms of caloric nystagmus (ENG CN), each of which was submitted to qualitative and quantitative evaluation. We concentrated mainly on atypical features in the ENG CN. Lengthy (over 5 s) pauses of nystagmus, marked tonicity (slow components lasted several seconds), impaired rhythm and form of nystagmic movements, presence

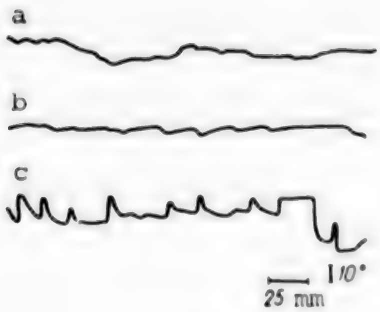

Figure 1.
ENG fragments with atypical signs: pauses in responses (a), tonicity (b), partial reversal of reaction (c)
Tracings made during bithermal test with Barany's symptom

of many reverse nystagmic movements or reversal of the entire reaction, as well as total absence of nystagmic beats on the tracing, were considered atypical. Examples of fragments of atypical reactions are illustrated in Figure 1.

In addition to caloric tests, we performed optokinetic tests with recording of optokinetic nystagmus (ENG OKN). We tested for two types of reactions, cortical (OKN (OKN_c) and subcortical (OKN_{sc}) using a previously described method [4-6]. The velocity of the optokinetic stimulus was 20°/s. In evaluating ENG OKN, we concentrated mainly on symmetry of reactions directed to the right and left. A total of 96 ENG OKN were analyzed.

Results and Discussion

There was a significant number of atypical reactions on the ENG CN (56 out of 96). The maximum number was demonstrated in caloric tests performed before the work shift: 4 out of every 5 ENG had atypical elements. In the sample of ENG CN recorded after work, atypical reactions constituted less than half (19 out of 48). This finding enabled us to assume that there is a tendency toward normalization in the "evening" responses. This assumption was confirmed when we compared pairs of "morning" and "evening" results in the same caloric tests on each subject. A change in the direction of normalization, i.e., decrease in number of atypical signs, was designated with a plus sign, and progression of atypical elements was designated with a minus sign; absence of visible changes was designated by a zero. Each line in the table corresponds to the results of testing one subject, while each column refers to result of comparing morning and evening data for the same tests: 1--cold, on the right; 2--cold, on the left; 3 and 4--warm on the right and left, respectively. In addition, columns 5 and 6 list the results of evaluating optokinetic reactions of the same subjects.

Comparison of results of morning and and evening tests (explained in the text)

No	Bithermal test				Optokinetic test	
	cold		warm		OKN_c	OKN_{sc}
	1	2	3	4	5	6
1	0	0	+	+	<	>
2	+	-	0	+	<	>
3	0	+	—	+	<	?
4	—	+	+	+	<	<
5	+	0	+	+	>	>
6	+	+	+	+	<	>
7	+	—	—	+	<	>
8	+	+	0	+	0	<
9	+	—	+	+	<	<
10	+	+	+	+	?	<
11	-	0	+	+	<	>
12	+	+	+	+	<	<

Figure 2 illustrates fragments of ENG that explain the meaning of paired comparison of responses. In the first pair (Figure 2a), both ENG are atypical; they contain reversed nystagmic beats. Such a result was designated by a "0" (see Table, line 1, column 1). The second pair (Figure 2b) is an example of a shift in the direction of

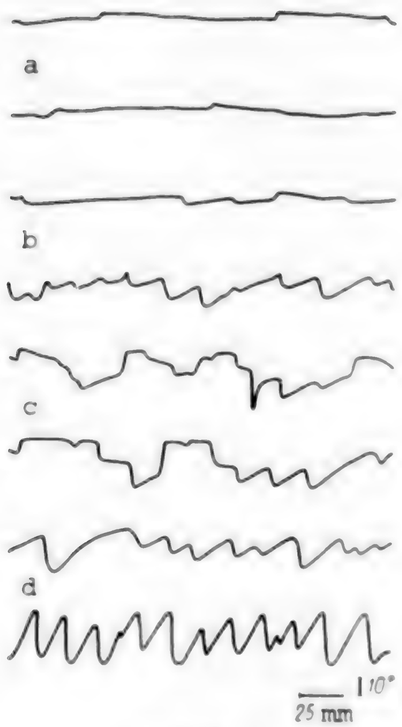

Figure 2.
Fragments of ENG recorded in caloric tests
Comparison of pairs of reactions: to cold test on the left (a), warm test on the left (b), cold test on the right (c) and warm test on the right (d). Other explanations given in the text

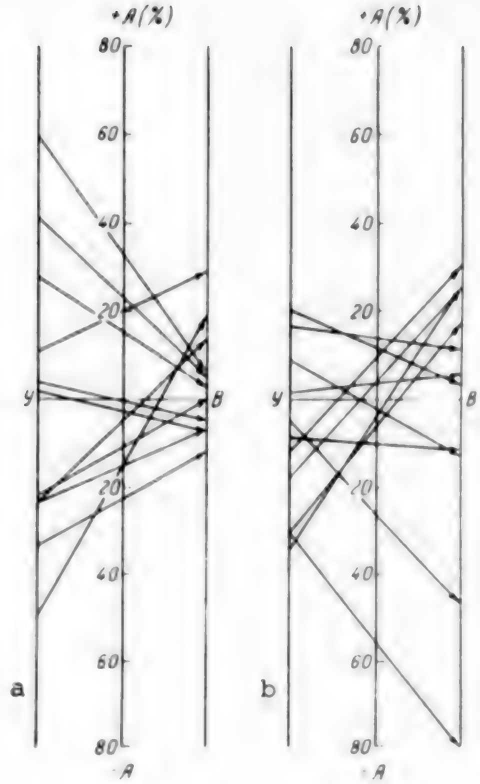

Figure 3.
Asymmetry (A) of cortical (a) and subcortical (b) optokinetic reactions during morning and evening tests

normalization, since atypical signs were found only in the morning ENG. This result is designated by a plus sign (see Table, line 1, column 4). Figure 2c illustrates more marked atypical signs: the evening reaction, unlike the morning one, is inhibited and consists of separate beats alternating with long pauses. The result of comparison is designated by a minus sign (see Table, line 11, column 1). Figure 2d illustrates normalization of rhythm in the evening response (see Table, line 5, column 3).

Having used a nonparametric criterion (for example, sign criterion [13]) to interpret the data (see Table), it can be maintained (with less than 1% probability of judgment error) that the evening reactions generally differ from morning ones: only 7 zeros in 48 pairs. This cannot be considered a chance finding. It can be stated with the same level of reliability that changes in the direction of normalization of caloric nystagmus are typical. Excluding the zeros and considering the smaller sample, we can become convinced that the small number of minus signs (only 7 in 41 pairs) does not warrant the belief that prevalence of plus signs is a chance occurrence.

Functional changes in the vestibular system under the effect of vibration, which are associated with impaired forms of nystagmus, cannot of course occur without involving its central elements; however, changes also apparently occur in the receptor system of the labyrinth in the course of the work day. This can be elicited on the basis of changes in coefficient of labyrinthine asymmetry (LA), a traditional parameter calculated from the results of the bithermal test, which is directly related to the state of the peripheral level [6]. It was possible to obtain such an evaluation only in 7 subjects, since the LA could not be calculated for the others due to the atypical nature of some reaction or other on the ENG. The LA coefficient remained unchanged in only two cases, and in both instances it equaled zero in both the morning and evening tests. In the other 5 cases, LA changed in value and sign in the course of the day. Here are a few examples: in the first subject (see Table, line 1), LA changed from -16 to +52%; in the second, from +4 to -22% and in the 5th, from -27 to 0%.

Substantial changes were also demonstrated in optokinetic responses. Calculation of relative asymmetry of intensity (mean velocity of slow component) in each pair of OKN in opposite directions, followed by comparison of asymmetry in the morning and evening reactions of each subject served as the basis for analysis of these reactions. The results of this comparison are listed in the table (columns 5 and 6), where changes are shown that occurred in OKN asymmetry in the course of the work day: the symbol > refers to increased asymmetry, < to decrease and 0 to absence of change. In two cases (with a question mark), this approach could not be used since both morning subcortical optokinetic reactions were reversed in one subject and in the other, both cortical morning responses were reversed. We succeeded in comparing morning and evening responses in 22 pairs. Changes in asymmetry were found in 21 cases. This warrants the statement that this finding is statistically reliable. It is interesting to examine the same material from the standpoint of assessing the direction of change in asymmetry, and this can be well-seen in Figure 3. For OKN_c, changes in the direction of less asymmetry in the evening reactions prevailed with statistical reliability over morning reactions; normalization occurred in 9 out of 10 cases. No statistically reliable changes in asymmetry were demonstrable for OKN_{sc}.

Thus, changes occur in the vestibulo-optokinetic system of individuals who are regularly exposed to industrial vibration; they are manifested by atypia and asymmetry of nystagmic reactions; atypical may be rather significant (even a reversal), while asymmetry reaches 50% and sometimes more. The most marked changes are demonstrable according to the results of tests performed before the work shift. Conversely, after work, there is a tendency toward normalization of nystagmic reactions. The following can be expounded as a working hypothesis on the origin of the "normalization phenomenon." Vibration affects both the central elements of the vestibular system (atypical reactions and peripheral ones (changes in LA coefficient). Exposure to vibration is associated with immediate and delayed effects. The former are similar to the effect of stimulation; they are related to the direct effect of vibtation on the receptor system and are relatively brief, since they depend on the duration of exposure [7, 8]; the latter are attributable to processes similar to cumulative effects. Expressly these delayed effects influence the state of all levels of the vestibular system, lowering its reactivity, altering characteristics of nystagmus and causing impairment of its form, to the extent of reversal. In

other words, the changes demonstrable on morning nystagmograms are the result of the delayed effect. The immediate effect, however, is manifested in individuals of the tested category by distinctive acceleration of the already altered system, as a result of which there is a tendency toward normalization in the course of the work shift.

The normalization phenomenon adds to the range of objective symptoms inherent in vibration sickness. Also noteworthy is the fact that the vestibulometric results on individuals exposed to vibration are a marked function of time at which the vestibulometric tests are performed, and one cannot fail to take this into consideration in the practice of professional screening and expert professional evaluation.

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MOTHER-FETUS SYSTEM AS OBJECT FOR INVESTIGATION OF MECHANISMS OF PHYSIOLOGICAL EFFECT OF WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 28 Jul 86) pp 63-66

[Article by L. V. Serova]

[English abstract from source] The place of embryological investigations in the program of mammalian experiments onboard the Cosmos biosatellites is discussed. The mother-fetus system is viewed as a specific loading test for studying the reserve potentials of the mammalian body in microgravity. It has been demonstrated that mammalians (Wistar rats) flown during the third term of their pregnancy can maintain homeostasis of the developing fetus within the limits that provide the normal development of physiological functions. Significant individual variations in animal responses to microgravity have also been found.

[Text] Investigations with use of animals aboard biosatellites of the Cosmos series were begun at a time when it was already clear than man can live and work rather efficiently in weightlessness. Extensive material has been accumulated concerning the effects of spaceflight factors on various aspects of human vital functions [2-5, 9-11, 13, 20, 21]. Still, there are still many questions left unanswered.

Still open was the question of the price of adaptation of weightlessness: Is it associated with discrete pathological changes in internal organs, adverse long-term sequelae and reduced life expectancy? I. V. Davydovskiy wrote on this score: "Man has conquered pain and fear, he has proved that existence in weightlessness is possible.... True, man cannot yet indicate the price at which he achieves new, higher forms of adaptation" [8, p 303].

This basic question could be answered only on the basis of planned and systematic experiments with animals, primarily mammals, flown in spacecraft for different periods of time. Only such experiments could permit a comprehensive study of the structure and metabolism of different tissues in weightlessness, use of diverse load tests, including rather complicated ones, study of long-term consequences of flight factors and, finally, determination of statistical significance of the obtained data.

Investigations aboard specialized Cosmos biosatellites began with evaluation of the condition of animals, male Wistar rats, which were at relative rest during spaceflight and in the recovery period, without additional loads. The stress reaction on the day of completion of the flight was moderate, while changes in the skeletomotor system, myocardium, erythrocyte system, which developed in flight, were reversible, and had disappeared entirely by the 25th day of the recovery peirod [6, 7].

Diminished motor activity, distinctive functional hypokinesia that facilitates readaptation to earth's gravity following exposure to microgravity, was one of the main adaptive reactions of animals returned to earth after a spaceflight. It seemed probable that if even the most insignificant load situations were produced in the postflight period we would encounter their poorer tolerance in flight group animals, primarily with impaired functional coordination of systems that maintain homeostasis in the presence of loads [16-17, 25].

However, studies conducted at the next stage, with postflight use of rather intensive functional tests, failed to confirm this assumption. From the very first day of the recovery period, tolerance to immobilization stress tests was quite satisfactory, while the responses to a series of repeated tests (decrease in weight of the body, thymus, spleen and in number of thymocytes and splenocytes, concentration of corticosterone in blood and the adrenals, etc.) were virtually the same in experimental and control groups [18, 24].

Having obtained these results and constructing the logic of investigation on the gradual complication of load situations imposed on animals, we undertook a search for an even more universal test that would require, on the one hand, mobilization of reserves and strain on all regulatory systems (similarly to a stress test) and, at the same time, would provide a specific load for different organs and systems, in which rather marked though reversible changes occur in weightlessness (bone, erythrocyte system and others). In the quest for such a universal load test, it occurred to us that it would be expedient to use the mother-fetus system as an experimental model for investigation of the mechanisms of physiological effects of weightlessness and, first of all, to asess compensatory and adaptive capacities of living systems under such conditions. Our choice was based on the fact that pregnancy is related to a need for significant activation of anabolic processes, mobilization of calcium to build the fetal skeleton, activation of the erythrocyte system and several other changes, that are the exact opposite of the changes observed under spaceflight conditions. We assumed that the effect of weightlessness on the fetus surrounded by amniotic fluid would be transmitted through the maternal organism, being determined by its metabolism and hormonal status.

These theoretical premises served as the basis in preparing and conducting the first embryological experiment with mammals during a spaceflight aboard Cosmos-1514 biosatellite.

For this experiment, we used 10 Wistar rats which spent the 13th to 18th day of the gestation period in weightlessness, as well as animals used for vivarium, synchronous (in a ground-based mock-up of a biosatellite) and baseline (dissected on the day of the launch) controls.

In accordance with the program, on the day the flight was terminated 5 flight group rats were dissected and about 60 fetuses were obtained from them for the studies. Five females were left until natural parturition; they produced about 50 liveborn offspring, which were kept under observation for several months until they reached sexual maturity.

The results of the experiment warrant the conclusion that animals exposed to weightlessness are capable of activating compensatory and adaptive processes, as well as mobilization of necessary reserves for normal fetal development [26, 27]. In spite of rather serious changes that occurred in the mothers, an integral expression of which was about 25% weight loss in 5 flight days, there was virtually no change in parameters of reproductive function. Fetus from flight group animals showed slight developmental retardation, as manifested by retarded weight gain and development of ossification regions of the skeleton, reater relative fluid content in fetal tissues. However, the differences between groups were insignificant (±10%) and soon disappeared: newborn rats delivered 5 days after return to earth no longer weighed less than animals in the synchronous control, and they were even ahead of the control group rats in size of ossification centers. Interestingly, total weight of fetuses that developed in weightlessness born to each female was the same as in the vivarium control: 11.40 and 11.47 g, respectively. This means that, in spite of the fact that the females showed significant weight loss due to intensification of catabolic processes in weightlessness, the flight group of animals activated anabolic processes related to fetal growth to the same extent as control rats. While nursing their offspring, the flight group of rats retained normal maternal behavior and provided the required amount of milk. In the postnatal period (until they reached sexual maturity), the rate of body and organ weight gain was virtually the same in experimental and control groups.

Since exposure to weightlessness and pregnancy (each in itself) is associated with serious changes in metabolism of fluid and electrolytes (primarily calcium), when planning the experiment we expected that the combined effect of these two factors would be associated with serious and perhaps even catastrophic changes in calcium metabolism. Indeed, we found a substantial (over 50%) decline in calcium content of the liver and kidneys of flight group female rats. Fewer changes were observed in the skin and virtually none in bone ($p>0.05$). The maternal organism was able to provide for homeostasis of the developing fetus: concentration of sodium, potassium, calcium and magnesium in its tissues as scaled to the unit of dry weight were the same in the experiment and controls both on the 18th day of the gestation period (day of termination of flight) and at the early stages of postnatal ontogenesis. Absence of serious differences beween experiment and control in development of the central nervous system and analyzers is also indicative of highly efficient maintenance of fetal homeostasis during the flight.

Necropsy on animals that spent part of the prenatal period in weightlessness on the 15th, 30th and 100th day of life failed to reveal differences between experimental and control groups with respect to weight of internal organs, metabolism of fluid, electrolytes, fats, nucleic acids and biologically active substances [1, 12, 26, 27], i.e., exposure to weightlessness in the fetal period at the stage of formation of internal organs and mechanisms regulating their activity did not affect the rate of growth of organs or level of

metabolism in them at different stages of postnatal life until the animals reached maturity. The only serious difference between experiment and control was a change in metabolism of collagen in the skin and bone of animals that developed in weightlessness, which is indicative of some delay in development of connective tissue [14]. Presence of these changes in both the mothers and offspring at all stages of development (up to the age of 3 months), as well as the similarity of changes observed in the skin and bone, are indicative of their systemic nature, and they require further expansion of research in this direction.

The results of the embryological experiment aboard Cosmos-1514 and corresponding ground-based model experiments, which demonstrated the basic possibility of normal development of the mammalian fetus when the mother is exposed to weightlessness, are also indicative of the possibility of rather serious changes in some specimens. While most animals tolerated weightlessness without developing irreversible pathological changes and complications in the recovery period, some specimens presented serious changes (for example, such as stillbirths in one of the flight group females or birth of weak rats that died in the first days of life) [26].

The very fact that individual differences exist in responses to environmental factors (including weightlessness and hypergravity) is not new; it has been discussed and analyzed by a number of authors [8, 11, 22, 28, 29].

It can be assumed that individual differences arise due to gradually accumulating changes in the genetic system (for example, when animals are kept in the vivarium without exposure to additional factors), which remain neutral or virtually neutral for a long time [23], i.e., which have no significance to the fate of the individual or population as a whole. In stress situations, these differences are apparently the basis for differentiation of animals according to resistance, whereas in the case of extreme factors they could lead to death of some of them.

There is basic biological significance to separation of animal populations into distinct, quantitatively rated groups that differ appreciably in resistance to diverse environmental factors, which determine the dynamics of survival under ordinary conditions [15, 19], onset, course and outcome of diseases [8].

With reference to the relevance of individual resistance and reactivity to problems of long-term spaceflights, it is worthwhile to recall the studies of R. Burton and A. Smith [22, 28], who obtained more than 20 generations of birds in 2 G hypergravity. Already in the first generation, there was a certain percentage of specimens that poorly tolerated hypergravity, while selection, as usually occurs in nature, occurred on the population level by means of crosses between specimens that adapted better than others to changes in environmental conditions. Apparently, similar findings would be made if one tried to obtain several generations of animals under spaceflight conditions. For this reason, one of the goals of future research is to find methods of preliminary (preflight) prediction of individual reactions of different specimens to weightlessness.

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SPLEEN LYMPHOCYTE NUCLEIC ACIDS IN PREGNANT RATS FLOWN IN SPACE AND THEIR OFFSPRING

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 4 Aug 86) pp 66-69

[Article by G. S. Komolova, V. F. Makeyeva, I. A. Yegorov and L. V. Serova]

[English abstract from source] The spaceflight effect on the synthesis of nucleic acids in spleen lymphocytes in pregnant rats and their offspring was investigated. In addition to the inhibition of the DNA replicative function previously detected in males, activation of RNA synthesis was seen in the pregnant females. Such changes did not develop in the synchronous mock-up controls. The 30-day and 100-day old pups of the rats flown in space during the last third of their pregnancy showed no changes in the DNA replicative function. The 100-day old animals displayed only a slight, when compared to the vivarium controls, decline of RNA synthesis which was produced by concomitant factors rather than by microgravity per se. It is supposed that microgravity-induced activation of RNA synthesis in spleen lymphocytes of pregnant rats is associated with the involvement of these cells in adaptive trophic processes that are to maintain plastic homeostasis of the fetus in an unusual environment.

[Text] Experiments aboard biosatellites of the Cosmos series established that prolonged weightlessness does not elicit serius metabolic disturbances in animals [1]. At the same time, irreversible functional changes do occur. They may be related to both acute stress responses to dynamic flight factors and chronic processes that develop in weightlessness due to lack of load on the skeletomuscular system.

Lymphocytes play an important role in maintaining plastic homeostasis in stress situations [2], and for this reason it is interesting to have information about metabolism of nucleic acids and proteins in lymphoid tissues in order to disclose the mechanism of formation of adaptive reactions.

Previously, inflight and model experiments were conducted to investigate the effects of spaceflight factors on nucleic acid metabolism in cells of male rate lymphoid organs [3, 4]. Here, we submit the results of an embryological experiment conducted aboard Cosmos-1514 biosatellite pertaining to investigation of DNA and RNA synthesis in spleen lymphocytes in the mother-fetus system.

Methods

In our study we used Wistar rats. In the experiment, 10 females in the last trimester of pregnancy were flown for 5 days.

In control studies, we adhered to the conditions that applied for experiments of the Cosmos series, which enabled us not only to demonstrate the effects of the set of spaceflight factors as a whole, but to distinguish the role of weightlessness [5, 6]. For this purpose, we ran two ground-based controls: vivarium--animals kept in the vivarium on the same water and feed allowance as those in flight; synchronous--animals that were kept not only on the same diet, but exposed to simulation of all physiologically relevant factors of the "atmosphere" and "landing" phases in a spacecraft (vibration, accelerations, impact accelerations, noise).

On the day of termination of the flight (18th day of pregnancy) 5 rats were decapitated and material taken from them for examination. The other 5 rats were left to the time of natural parturition. The offspring obtained from them was then examined at the age of 30 and 100 days.

We determined the rate of nucleic acid synthesis in spleen lymphocytes according to incorporation of radioactive precursors: 5-methyl-^{3}H-thymidine (specific activity 370 mCi/mmol) in DNA and 5-^{14}C-uridine (specific activity 270 mCi/mmol) in RNA. A previously described method was used [4] to isolate lymphoid cells from the spleen and test them for uptake of radioactive precursors in nucleic acids. Radioactivity of nucleic acids was calculated for DNA, and their concentration was determined with a spectrophotometer [7].

Results and Discussion

As can be seen in Figure 1, in the flight group of animals there was less replication of DNA in spleen lymphocytes than in the vivarium control, by a factor of almost 2, whereas in the synchronous experiment rats there were no statistically reliable changes. It is important to note that a decline in DNA biosynthesis in spleen cells under the effect of flight factors, as was previously established, also occurs in male rats [3], and consequently this is not inherent solely in pregnant animals. The most probable assumption is that the changes in replicative function of DNA in the tested cells when the animals are exposed to weightlessness for a long time are attributable to chronic stress, which develops in the nature of a hypokinetic syndrome due to lack of load on the skeletomuscular system.

Model experiments revealed that spleen lymphocytes react to long-term hypokinesia by depression of synthesis of nucleic acids and proteins [4]. Consequently, pregnancy, which may be viewed as an additional functional load under spaceflight conditions, has no appreciable influence on the nature of the stress reaction of the DNA-synthesizing system of spleen lymphocytes.

The inhibition of DNA synthesis in cells of rat lymohoid organs initiated by spaceflight factors is reversible, and the process usually reverts to normal in the recovery period [3].

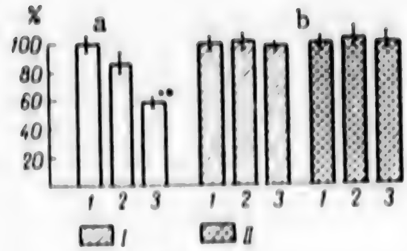

Figure 1.
Intensity of ^{3}H-thymidine uptake in spleen lymphocyte DNA of rats (a) and their offspring (b)
Here and in Figure 2:
I, II) age of offspring, 30 and and 100 days, respectively
1) vivarium control
2) synchronous control
3) flight experiment
Asterisks and circles show reliable differences from vivarium and synchronous control, respectively

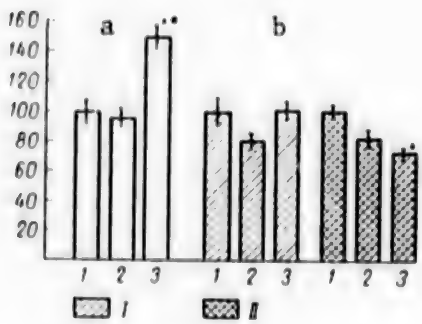

Figure 2.
Intensity of ^{14}C-uridine uptake in RNA of lienal lymphoid cells of rats (a) and their offspring (b). Designations are the same as in Figure 1

As can be seen in Figure 1, there were no disturbances of replicative function of DNA in lienal lymphocytes in the offspring of rats flown in space in the last trimester of the gestation period. In both 30- and 100-day old offspring DNA synthesis in lienal lymphocytes did not differ reliably from the appropriate age-related controls.

Investigation of RNA synthesis in spleen lymphocytes of pregnant rats flown in space revealed some distinctions. As can be seen in Figure 2, in pregnant animals of the flight group, RNA synthesis was higher than in the control groups. Absence of activation of RNA synthesis in lymphocytes of the vivarium control groups of animals may be indicative of the fact that the intensification of DNA transcription function in flight was caused by weightlessness.

The fact that the effect occurs in the presence of diminished replication indicates that it does not occur through intensification of template DNA synthesis. At the same time, we cannot rule out intensification of transcription of certain loci in the genome, which should lead to an increase in level of transcripts of some type or other.

In particular, we cannot rule out intensified production of stable RNA, since the RNA/DNA ratio in the cells increased by more than two times.

RNA synthesis in lienal lymphocytes held at the normal level in 30-day old offspring (see Figure 2b), but it was reliably 28% diminished in 100-day-old ones, as compared to the vivarium control. In the synchronous experiment, animals of both age groups also presented a tendency toward decline of this parameter. The differences between the flight experiment and synchronous control were not substantial for the 100-day rats.

Considering that all physiologically important spaceflight factors were simulated in the synchronous experiment, it should be concluded that the depression we observed in RNA synthesis in lienal lymphocytes in offspring of experimental rats may be related to nonspecific stress-producing effects on the mother in the period of landing the spacecraft. As for weightlessness, its significance does not appear to be significant to the phenomenon in question.

In view of the fact that lymphocytes play an important part in trophic processes, it can be assumed that activation of RNA synthesis in lienal lymphoid cells of pregnant animals induced in flight by weightlessness is directed toward preserving plastic homeostasis of the fetuses. Absence of consequences referable to the parameters under study in offspring of pregnant animals exposed to weightlessness is a reflection of this correlation.

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DISTINCTIVE CHANGES IN ARTERIAL PRESSURE AND BLOOD FLOW IN COMMON CAROTID ARTERY OF MONKEYS FLOWN ABOARD COSMOS-1514 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 11 Oct 86) pp 69-74

[Article by V. P. Krotov, H. Sandler, A. M. Badakva, J. Hines, V. S. Magedov and H. Stone (USSR and United States)]

[English abstract from source] Preflight the rhesus monkey Bion was implanted with sensors and transducers to measure blood pressure and linear flow velocity in the common carotid artery and to compare these parameters with central circulation. At the early flight stage blood pressure increased, blood flow decreased and resistance in the area grew. The last change can be regarded as a compensatory reaction that can provide rapid adaptation of regional circulation to changes in systemic circulation. At later flight stages blood pressure showed distinct circadian oscillations and blood flow, a significant increase when compared to the ground-based 36-hour control study. Regulatory mechanisms of the cardiovascular system changed to the greatest extent on flight day 2. This manifested as a decrease of the amplitude of circadian oscillations of the above circulation parameters. Signs of cardiovascular adaptation to the effects of microgravity were discerned on flight days 3 to 5.

[Text] The data accumulated concerning responses of the cardiovascular system in weightlessness indicate on the whole the adaptive nature of dynamics of the basic circulatory parameters [1]. At the same time, there are reports of increased variability of these parameters, marked individual features in the process of circulatory adaptation and retention to the end of a flight of a number of adverse phenomena, supposedly related to distinctions of regional circulation under such conditions [3]. All this indicates that the essence of circulatory change in weightlessness, which we try to comprehend on the basis of measuring different parameters of central circulation, has not yet been revealed. In addition, medical studies of the effects of weightlessness are conducted under conditions where the adaptation process is corrected by means of preventive agents in order to preserve cosmonauts' health and work capacity, while the studies themselves are limited as to time and methodological feasibility.

A heavy-headed sensation, a feeling that the head is "stuffed," is a typical symptom that occurs at the very start of exposure to weightlessness. This is associated objectively with soft tissue edema of the face and neck to varying extents. It is believed that these effects are attributable to redistribution of circulating blood, with increased filling of vessels of the head and thoracic organs [6]. However, there are still only isolated data concerning the dynamics of blood flow to the head and its relation to circulation volume (CV), not only in weightlessness, but model experiments that reproduce redistribution of body fluids, which is a typical effect of microgravity. In particular, the French cosmonat, E. Chretien, who measured flow in the left carotid artery once a day using a Doppler flowmeter aboard the Salyut-7 station in the course of a 7-day mission, observed a 6% increase only at the first reading made on the 2d day of the flight [2].

The purpose of our experiments performed on monkeys during a flight of the Cosmos-1514 biosatellite was to obtain data on dynamics of blood supply to the brain and soft tissues of the head at the first and transient phases of adaptation to weightlessness, and its relation to central circulatory parameters.

Methods

We conducted this study on 8 Macaca mulatta monkeys 3.5-5 years of age, weighing 3.5-4.6 kg. Hemodynamic parameters were recorded by means of pre-implanted sensors and electrodes. Taking into consideration the results of pathoanatomic examination of the monkey called Bonnie, in which fresh and organized thrombi were found in pulmonary arteries and veins after flight aboard Biosatellite-3 [7], we decided to forego catheterization of vessels. We used extravasal sensors in the form of cuffs implanted on vessels. The measuring equipment, including a tensometer to measure arterial pressure (BP) and ultrasonic Doppler tensometer to measure linear blood flow velocity (LFV), was developed by American specialists of the Ames Research Center at NASA. Implantation of sensors on the left common carotid was effected by Soviet specialists under the leadership of Prof V. S. Krylov (All-Union Surgical Research Center, USSR Academy of Medical Sciences). The operation was performed in two stages: at the first stage, the BP and LFV sensors were implanted, and the wiring from them was subcutaneously guided to the back and placed in the region of the left scapula; 3-4 weeks later, the second stage of the operation was performed--bringing the wires out and implanting electrodes to record the ECG in the Nehb lead and to measure cardiac output with an impedance plethysmograph. The studies began 2-3 weeks after the second stage of the operation. Individual distinctions in regulation of circulation were assessed while the monkeys were kept for 1.5 days in a Bios-Primate capsule and by means of a functional postural test. On the basis of the results of the preflight examination, candidates were selected for participation in the flight. The condition of the circulatory system in flight was studied on a monkey named Bion.

The signals during the flight and in 1.5-day control tests were recorded on tape for 5 min at a time every 2 h. To expedite and objectivize signal processing, we used an automated system programmed to process parameters of the cardiovascular system.

It was initially assumed that the information would be processed for the entire 5-min period of recording with averaging per 20 cardiac cycles. However, analysis of inflight tracings revealed that there was significant "interference" in the signals due to the animal's motor activity. For this reason, we used the method of expert evaluation. For signal processing, we selected the recording periods when the animals were calm, as could be determined from the rheoplethysmographic curve and its first derivative.

We used the procedure of symmetrical sliding smoothing of 3 points to process results of readings obtained at 2-h intervals. To eliminate circadian fluctuations, we used a symmetrical sliding smoothing for 12 points, i.e., for 24 h. This procedure does not lead to phasic distortions of fluctuations that are slower than circadian [5]. The information obtained in flight was compared to prelaunch data and those from the 1.5-day study conducted before the flight. Unfortunately, we were unable to assess the reliability of circulatory system compensatory mechanisms during exposure to spaceflight factors (mainly weightlessness) by means of postflight functional tests on Bion, due to the fact that this monkey died of ileus 69 h after returning to earth.

Results and Discussion

As can be seen in Figure 1, in the course of the 1.5-day control experiment the recorded parameters for Bion decreased, particularly in comparison to the first readings, which is apparently related to decreased psychoemotional stress due to immobilization of the monkey in the chair and placing it in the Bio-Primate capsule in isolation from the outside world.

In the last 24 h of the control period, BP was in the range of 86 to 107 mm Hg, constituting a mean of 97.2 mm Hg; LFV varied from 14.6 to 27.3 cm/s in this period, averaging 20.4 cm/s.

Remaining in the rocket at the launch pad for 24 h was not a marked stress factor for the monkey. BP and HR [heart rate] (98.3 mm Hg, and 94/min, respectively) did not differ from control values. However, it should be noted that, before the launch, LFV increased on the average to 28.0 cm/s, which was 38% above the control level. Environmental factors that could have stimulated blood flow (temperature elevation and increase in CO_2 concentration in the biosatellite cabin) were ruled out, since there was no appreciable change in microclimate and gas composition of the atmosphere in the cabin in the prelaunch period. The cause of the noted increase in blood flow is not clear.

Immediately after insertion of the biosatellite into orbit, there were two powerful factors that affected the animal: removal of gravity and aftereffect of lift-off accelerations. Analysis of the results of model experiments, in which the monkeys were rotated on a centrifuge in the "lift-off" mode, enabled us to assess the effect of the latter factor on the circulatory system. While blood flow and BP changed significantly during rotation on the centrifuge, they showed virtually no difference from the baseline at the moment it stopped and reverted to normal within the next 1-5 min. Consequently, apparently it is expressly removal of gravity that should have a greater effect on circulatory parameters recorded a few minutes after insertion of orbit. As compared

to the prelaunch period, Bion's circulatory system virtually failed to respond to weightlessness: BP rose by less than 10%, and LFV decreased by only 4%.

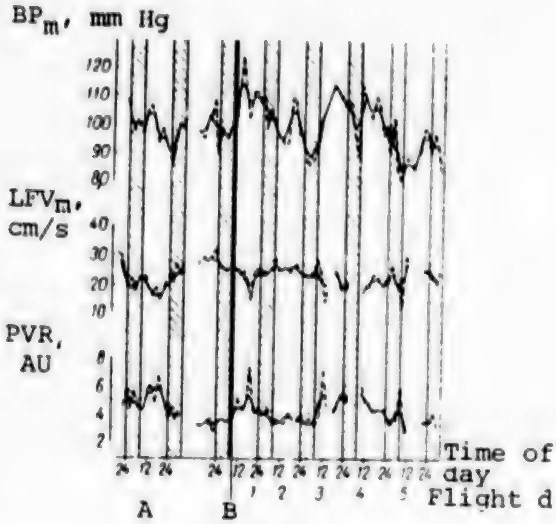

Figure 1.
Dynamics of inflight changes in BP, LFV and PVR [peripheral vascular resistance] in Bion

Here and in Figures 2 and 3:
A) control AU) arbitrary units
B) lift-off

Striped band corresponds to night time. Dash line shows data obtained from primary processing of material and the boldface line, the same after symmetrical sliding smoothing for 3 points

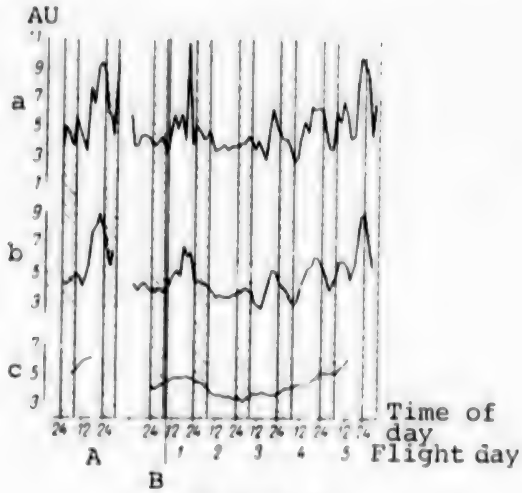

Figure 2.
Dynamics of correlation of LFV to the head and CV of Bion in control experiment and during flight
a, b, c) data obtained in primary processing of data, as well as after procedure of symmetrical sliding smoothing for 3 and 12 points, respectively

However, the original tendencies of reactions of circulatory system parameters continued to progress, and they were manifested by rather noticeable deviations from prelaunch values after a few hours of flight: BP rose by 16-27%, LFV decreased by 28%. By the end of the 1st flight day, there was a tendency toward normalization of the tested parameters.

A comparison of dynamics of changes in BP during the flight and in the control experiment enabled us to rule out an emotional response to change in the situation as the cause of BP elevation in Bion. Evidently, the hypertensive reaction observed in Bion for the first few hours of flight could have been due to weightlessness, in particular, redistribution of body fluids, primarily blood, in a cranial direction.

At the beginning of the flight (for 8 h), concurrently with BP elevation Bion showed decrease in LFV in the common carotid. In the postural tests, which were performed on monkeys under ketamine anesthesia, it was established that LFV exceed the baseline value by 10-20% only for 5-10 s after moving the animal to head-down position (70° tilt angle); already 1 min later, it constituted 90-95% of the baseline and remained on this level to the end of the

3-5-min observation period. It can be assumed that, immediately after insertion into orbit, LFV in the carotid increased for a rather short time (in this period, the aftereffect of head-pelvis accelerations was still there). However, by the time inflight LFV began to be recorded, after a few minutes of exposure to weightlessness, its value was already below the prelaunch level.

Marked increase in vascular resistance to flow in the system of the common carotid artery, which limited influx of blood to the head and plethora of vessels of both the brain and soft tissues of the head in the presence of its impaired efflux, was the result of opposite changes in BP and LFV in Bion in the first hours of flight. The possibility of impairment of efflux is indicated by the data obtained both in flight and in model experiments concerning elevation of central venous pressure (CVP) when blood shifts in a cranial direction. In Bonnie, pressure in the vena cava rose from 0.25 to 3.0 mm Hg on the 1st flight day; thereafter there was a tendency toward normalization on the 8th day of weightlessness [7]. In the model experiments, when records were made 5 min after moving the subject from horizontal to antiorthostatic position at an angle of -75°, pressure in the superior bulb of the internal jugular vein rose from 2.8 to 32.2 mm Hg, while CVP rose by 2-3 mm Hg. The higher pressure in antiorthostatic position also persisted in experiments on dogs, when duration of antiorthostatic position at -90° was increased to 3 h [4].

One of the manifestations of self-regulation of cerebral circulation is the protective sympathetic vasoconstriction of cerebral vessels, which provides for rapid adaptation of regional hemodynamics to changes in systemic hemodynamics. The increased resistance to blood flow in the common carotid artery, which was observed in Bion, could be expressly the compensatory process aimed at either preventing disturbances or normalization of cerebral hemodynamics.

On the next 4 days of flight, we could discern certain patterns in the changes in circulatory parameters. Dynamics of BP showed distinct circadian periodicity: elevation in the daytime and decline at night. However, we were also impressed by the fact that peaks of hypertension coincided with "operator" activity, which the monkey could not perform, for technical reasons in one case and due to inadequate training in another, and consequently it did not receive juice as a reward. In this case, we cannot rule out the additional stressor effect, since the monkey could have been nervous seeing that its partner received juice, and this could have led to more marked BP elevation. Also in favor of this assumption is the fact that, on the 4th day of the flight, after the monkey was able to obtain juice upon command from the ground and consumed it (100 mℓ), the range of BP fluctuations the following day diminished appreciably, and no elevation of this parameter was recorded during the period of performance of "operator" activity.

As already stressed above, in the control experiment and in the prelaunch period, BP values virtually coincided, but LFV differed appreciably. For this reason, when analyzing the inflight state, both values were taken into consideration, and it was possible to make more accurate comparison in the first hours of flight of LVF values to the period directly preceding lift-off, whereas for dynamics of blood flow over the entire flight, it is apparently preferable to make the comparison of its changes to those in the 1.5-day control experiment.

With this approach to analysis of the material, the mean LFV level was higher for the next 4 days than in the control.

The ratio of LFV to CV reflects the share of blood supply to the brain and, to a lesser extent, soft tissues of the head in the total pool of blood supply of the body. Considering that CV as a whole is determined by the oxygen requirements of organs and tissues, the range of which fluctuates rather significantly over a 24-h period, one can predict with certainty a decline of this ratio during the period of increased motor activity and rise at rest, which usually corresponds to the night, since there is a smaller range of fluctuation of blood supply to the head over a 24-h period than of CV. Hence, the value of this ratio can give us an idea about the function of the circulatory system under these conditions, while the range of fluctuations over a certain time is indicative of the extent of constitutional adaptation to changing conditions.

The lower value for this ratio in the prelaunch period, as compared to the control, implies that there is increase in circulatory system activity (Figure 2). The LFV/CV ratio was lowest as the 24-h mean on the 2d and start of the 3d day of flight. Then it increased, reaching the baseline level on the 5th flight day. The range of fluctuations of this ratio also depended on the stage of flight: being insignificant in the prelaunch period, it increased during the first hours of flight, diminished dramatically at the end of the 1st day, for the 2d day and start of the 3d. It then increased again, reaching a maximum level on the 5th flight day.

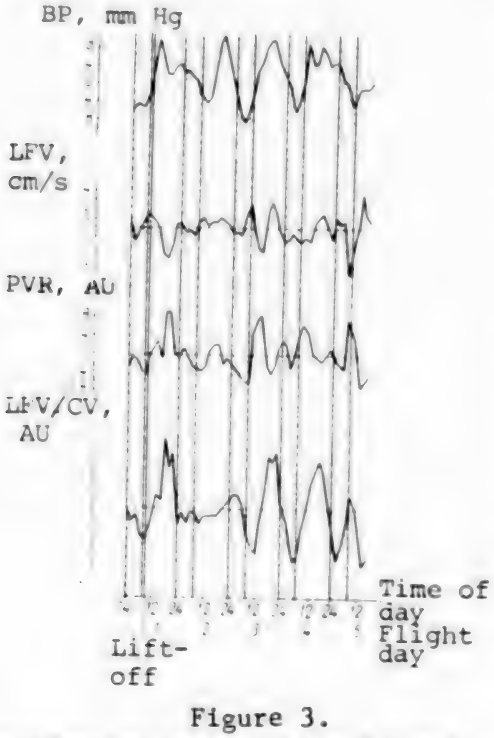

Figure 3.
Circadian pattern of circulatory parameters in Bion during flight

The decline on the 2d-3d day of LFV/CV and decrease in this time in the range of its fluctuations warrants the assumption that malcoordination of activity of regulatory mechanisms on different levels of control of the circulatory system arises at this stage, when there is exposure to the set of spaceflight factors. Starting on the 3d day of flight, the increase in range of fluctuations of the ratio over a 24-h period and elevation of its level may be indicative of development of the process of adaptation to weightlessness; presence of maximum amplitude of fluctuations on the last, 5th day of flight does not allow us to refer to complete adaptation of the monkey's system to weightlessness.

The circadian pattern of circulatory parameters we studied is indicative of inflight formation of a new level of neuroendocrine correlations to assure optimum function of the cardiovascular system in weightlessness. From the standpoint of general biology, cyclic processes in living systems, which include the circadian rhythm of parameters were are analyzing, can be viewed as adaptive processes aimed at maintaining equilibrium between the body and the

environment. For this reason, the decrease in amplitude of 24-h fluctuations of blood flow, PVR and LFV/CV may be indicative of change in function of regulatory mechanisms on different levels in the hierarchy of control of the circulatory system (Figure 3). The increase in amplitude of daily fluctuations is indicative of good adaptability.

After pursuing future studies on monkeys during an actual flight, it will be possible to judge the extent to which changes in hemodynamic parameters recorded for Bion in flight reflect the general pattern as to condition of the circulatory system in the acute period of adaptation to weightlessness.

Thus, in the first few hours spent in weightlessness by Bion, there was elevation of BP, decline of LFV to the head and increase in PVR in the common carotid artery. The latter can be viewed as a compensatory response called upon to assure rapid adaptation of regional hemodynamics to changes in systemic hemodynamics. On subsequent flight days, in the presence of marked fluctuations of BP over a 24-h period, there was an increase in blood flow to the head, as compared to the ground-based control.

The change in regulatory mechanisms of the cardiovascular system was the most marked on the 2d day of flight, as manifested by decrease in amplitude of 24-h pattern of the circulatory parameters studied. Signs of its adaptation to weightlessness appeared on the 3d-5th day of flight.

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BIOFEEDBACK CONTROL OF ALVEOLAR CARBON DIOXIDE TENSION TO ELIMINATE HYPOCAPNIA IN MAN IN THE PRESENCE OF HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 23 Jun 86) pp 74-77

[Article by I. S. Breslav, A. M. Shmeleva and A.T. Normatov]

[English abstract from source] Reactions of the respiratory system to the inhalation of a hypoxic gas mixture were compared when the test subjects (young healthy men) practiced normal breathing or breathing with a stable alveolar pCO_2. In the latter case the test subjects controlled their lung ventilation using the biofeedback technique. In this manner hyperventilation and related hypocapnia were eliminated. The possibility of practical application of biofeedback to the control of man's respiration in situations that may cause hypocapnia is discussed.

[Text] As we know, carbon dioxide tension (pCO_2) is one of the most important constants of the internal environment of a living system. Excessive flushing of CO_2 due to increased pulmonary ventilation leads to a number of adverse changes in physiological functions. Such changes occupy a definite place in the genesis of disturbances observed in the presence of hypoxic hypoxia [11-13, 15, 19]. Hypocapnia and related respiratory alkalosis lead to spasm of cerebral vessels (which could result in loss of consciousness and epileptic seizures), depress the activity of the central respiratory mechanism, particularly in individuals with a strong respiratory response to CO_2 [18]. As a result of these disturbances, there is aggravation of cerebral hypoxia and respiratory arrest may occur.

Many authors have recommended that the inhaled gas mixture be enriched with CO_2 to prevent hypocapnia during ascents to high altitudes or when breathing mixtures with low oxygen content [1, 8-10, 13]. However, as shown by mathematical modeling [5], this method requires precise dispensing of concentration of inhaled CO_2; it must be optimal for a given pO_2 drop in the respiratory environment, which is not always feasible.

Elimination of hyperventilation by means of voluntary control of breathing could be an alternate means of eliminating the hypocapnic change.

A method was developed in our laboratory to control human breathing by means of instrument-related feedback (biofeedback), which permits, in particular, stabilization of alveolar pCO_2 at a given level, without allowing change in this parameter under the effect of perturbing factors (for example, breathing through additional dead space) [2, 6, 14, 16]. We used this technique in our present study to prevent hypocapnic change in the presence of acute hypoxic hypoxia.

Methods

We conducted this study on 9 healthy men (average age 30.6 years, height 178.6 cm, weight 75.3 kg). Mean respiratory rate was 9.9/min, respiratory volume was 1.1 ℓ and minute ventilation was 10 ℓ.

Seated comfortably, the subjects breathed through a mask connected to a spyrographic attachment of the flow-through type, which automatically delivered respiratory mixtures (Figure 1) [4]. Electrical output of this device to an MN-10 analogue computer provided for recording pulmonary ventilation ($\dot{V}$), respiration rate (f), respiratory volume (V_I), duration of inspiration (T_I) and expiration (T_E). We also recorded maximum rate (first derivative) of build-up of negative pressure in the airways at the start of inspiration (dp/dt_I; t_I--current inspiration time). This parameter was used as a noninvasive indicator of respiratory center function, so-called initial inspiratory activity [17]. An MKh 6202 mass spectrometer was used for continuous recording of composition of alveolar gas.

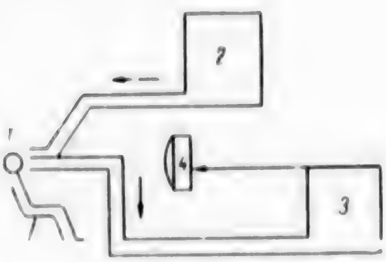

Figure 1.
Diagram of device for biofeedback control of alveolar p_ACO_2
1) subject
2) device for automatic delivery of respiratory mixtures and recording respiratory parameters
3) mass spectrometer
4) oscilloscope

After a control period of breathing ordinary air, for 5 min the subject breathed a gas mixture containing 11.1% O_2 in nitrogen, then switched again to air.

The study was carried out in two variants: the first, with free breathing and the second with stabilization of alveolar pCO_2 (p_ACO_2) by means of biofeedback control at the level recorded in the baseline period. In the second variant, the electric signal from the CO_2 channel of the mass spectrometer was fed to an oscilloscope, the screen of which was visible to the subject. In accordance with given instructions, the subject tracked the dynamics of his p_ACO_2 and controlled his breathing so as to hold this parameter at the specified level indicated by a marker on the screen.

Results and Discussion

As can be seen in Figure 2 and the table, during free breathing of a hypoxic mixture, p_ACO_2 dropped by a mean of 2.7 mm Hg by the 5th min (0.36 kPa); with biofeedback, however, this parameter showed virtually no change, although an insignificant transient decline was observed in the recovery period, when the subject ceased to voluntarily control his breathing.

Effect of hypoxia on respiratory parameters (M±m) during free breathing (B) and with stabilization of p_ACO_2 on control level by means of feedback (F)

Parameters	Conditions	Control (breathing air)	Breathing mixture with 11% O_2	Recovery (breathing air)
p_ACO_2, mm Hg	B	38,3±1,1	34,8±1,0	37,1±1,0
	F	38,0±1,2	38,5±1,1**	37,3±1,3
$\dot{V}_E$, ℓ/min	B	7,7±0,6	9,6±0,8	6,9±0,4
	F	7,8±0,6	8,6±0,5*	6,4±0,4
V_T, ℓ	B	1,21±0,14	1,38±0,16	1,12±0,17
	F	1,19±0,15	2,31±0,12**	1,29±0,17
f, cycles/min	B	7,7±1,2	8,3±1,3	7,5±0,9
	F	8,1±1,3	4,7±0,3**	5,8±0,6*
T_I, s	B	3,1±0,5	2,5±0,4	2,9±0,5
	F	2,8±0,4	3,8±0,4*	3,5±0,5
T_E, s	B	8,0±1,7	7,5±1,4	7,6±1,4
	F	7,8±1,6	13,1±1,2**	8,6±1,0
dp/dt_I, mm water/s	B	85±5	105±7	69±3
	F	87±5	172±31**	72±5

*Reliable differences as compared to same parameter recorded with free breathing at $p<0.05$.

**Same at $p<0.01$.

Let us compare the changes in respiratory parameters (see Table).

Without stabilization of p_ACO_2, hypoxia elicited some increase in ventilation due to slight increase in respiratory volume and respiratory rate, and there was shortening primarily of inspiration. Central inspiratory activity increased.

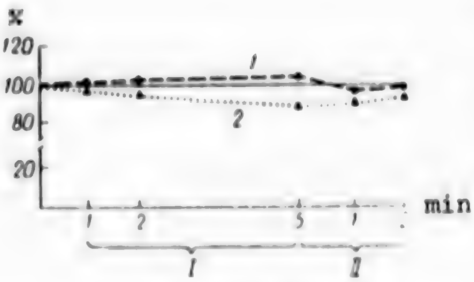

Figure 2.
Changes in p_ACO_2 during inhalation of hypoxic mixtures with free breathing (2) and with stabilization of p_ACO_2 on control level by means of feedback (1)
X-axis, time (min):
I) breathing mixture 11% O_2 in N_2
II) breathing air (recovery period)
Y-axis, p CO_2 (% of baseline)

With biofeedback control of p_ACO_2, the change to a hypoxic mixture was associated only with insignificant increase in ventilation. At the same time, we were impressed by the dramatic deepening of respiration with equally dramatic slowing, due to extension of both the inspiratory and particularly expiratory phase of the respiratory cycle.

Thus, in the desire to prevent increase in ventilation due to the hypoxic stimulus, the subjects involuntarily deepened it significantly. Such a paradoxical reaction is attributable to the distinctions of mechanisms that provide for reciprocity between flucutations of frequency and depth of respiration that occur at rest, which permits retention of a constant level of alveolar ventilation [3]. In this case, hypoxic stimulation also was instrumental in increasing

respiratory volume. This is confirmed by the steep increase in central inspiratory activity.

In spite of the counteraction of these regulatory mechanisms, the subjects succeeded in preventing appreciably increase in ventilation and thereby in preventing the hypocapnic change itself. Consequently, this method can be used in practice, training the individual to control his ventilation under hypoxic conditions. Of course, there is also a negative side to this procedure: elimination of ventilation response excludes on of the mechanisms for compensating the shortage of oxygen in the breathing atmosphere. Indeed, in our studies, alveolar pO_2 dropped to 48.7 mm Hg (6.48 kPa) when breathing freely a mixture containing 11.% O_2, and to 41.8 mm Hg (5.56 kPa) under biofeedback conditions. Apparently, the solution to this dilemma depends on which factor could be more detrimental to the body's functional state in some concrete case, hypoxemia or hypocapnia.

Of course, hypoxia is far from being the only possible cause of hyperventilation with excessive output of CO_2 and development of alkalosis with all the ensuing consequences. Thus, hyperventilation that occurs in man under stress may elicit disorders in the central nervous system and seriously impair his work capacity. Such situations have been described, for example, for pilots at important moments of their professional activities [7]. Special training to stabilize p_ACO_2, carried out by the biofeedback method, may also be beneficial in the matter of preventing dangerous complications of this nature.

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ROLE OF HEMOGLOBIN AFFINITY FOR OXYGEN IN EFFICIENCY OF BLOOD RESPIRATORY FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 14 Oct 86) pp 77-80

[Article by K. P. Ivanov, A. Ye. Chuykin, G. V. Samsonov and N.P. Kuznetsova]

[English abstract from source] In acute experiments the oxygen transport properties of two solutions of modified stroma-purified hemoglobin were investigated using anesthetized Wistar rats. The solutions were: solution 1 (Hb = 8.0 g per 100 g, P_{50} = 12.5mmHg) and solution 2 (Hb = 4.4 g per 100 g, P_{50} = 21.5 mm Hg). The solutions were used in stage-by-stage isovolumic substitution in rats of two groups. The modified hemoglobin solution with a lower hemoglobin oxygen affinity was found to be a more efficient blood substitute. In spite of its low oxygen capacity, it could sustain life activity at very low hematocrit values. When the oxygen capacity of blood is moderate or low, hemoglobin oxygen affinity plays a very important part in oxygen supply to different tissues, specifically to the heart. The latter determines the crucial compensatory physiological reaction to acute anemia, i.e. increase of cardiac output.

[Text] The efficiency of oxygen transport from the lungs to the capillaries of various organs and from capillaries to tissues is controlled primarily by changes in blood hemoglobin concentration, curve of oxyhemoglobin dissociation and blood flow rate. One of the most important problems of contemporary physiology of blood is to determine the quantitative value of each of these parameters and their optimum combination for various physiological states [1, 2, 4, 5].

Here, we tried to solve this problem by means of gradual replacement of animals' blood with synthetic oxygen-transporting blood substitutes prepared on the basis of modified hemoglobin. One of the blood substitutes had a high hemoglobin affinity for oxygen P_{50} = 12.5 mm Hg and hemoglobin concentration of 8.0±0.7 g/100 g blood substitute (solution 1); the other, P_{50} = 21.0±0.5 mm Hg, 4.4±0.6 g/100 mℓ (solution 2).

Methods

Experiments were performed on anesthetized (40 mg/kg sodium amytal intravenously) male Wistar rats weighing 250-300 g. We effected staggered (step-by step) isovolemic substitution of blood with the above-mentioned solutions of hemoglobin using a peristaltic pump through the femoral artery at the rate of 0.3 mℓ/min. In the baseline state and every 20 min after each substitution, we measured the animals' total gas exchange by means of an intubation cannula, which was introduced into the trachea and connected to a miniature Krogh apparatus. Gas composition of exhaled air was determined using an MKh6203 mass spectrometer produced by the USSR Academy of Sciences (Leningrad). We also determined oxygen tension (pO_2) in arterial and mixed venous blood from the animal's right heart (BME-33 blood microanalyzer, Denmark), oxygen content of arterial and mixed venous blood using the Lex-O_2-Con apparatus (United States), minute circulation volume (CV) (according to total oxygen uptake and arteriovenous difference for oxygen), curves of dissociation of oxyhemoglobin of whole blood, solutions 1 and 2, overall curves of dissociation of erythrocyte oxyhemoglobin administered with blood substitute to varying degrees of substitution (Hem-O-Scan apparatus, United States). In addition, we measured systemic arterial pressure, pH of arterial blood, CO_2 (pCO_2) tension in arterial and venous blood, heart rate, minute volume and respiration rate. Hereafter, we shall discuss only parameters necessary to analyze efficiency of blood respiratory function. Each experiment lasted 3 h. Throughout the period of the study, body temperature was held at 37±0.5°C. Viscosity of the solutions was virtually identical to that of blood: 1.90 and 1.35 cpoise for solution 1 and 2, respectively.

Solution 1 was given to 8 animals (1st group) and solution 2, to 10 (2d group).

Results and Discussion

The table lists the main physiological parameters required to analyze effectiveness of respiratory function of blood. According to this table, with 90% replacement of blood, the 1st group of animals showed decline by about 30% in total oxygen uptake. With 97% blood replacement, 6 animals died, and in the surviving ones overall oxygen uptake was half the baseline value. The rats in the 1st group showed 44% increase in CV with 45% replacement of blood with solution 1. Upon further replacement, their CV decreased. With 97% replacement of blood, the survival animals should CV of only 64% of the baseline value.

In the 2d group of rats, replacement of up to 97% of their blood did not alter the baseline level of oxygen uptake. Their CV increased continuously and at 97% replacement reached 204% of the baseline level.

As can be seen in the table, at all levels of substitution of blood, total blood oxygen content was 12-42% higher in the 1st group than in the 2d. This is attributable to hemoglobin's affinity for oxygen in solution 1 and the high concentration of hemoglobin in this solution. Thus, the efficiency of respiratory function of solution 1 in the lungs was considerably higher than that of solution 2. However, on the level of tissue capillaries, efficiency of respiratory function of blood depended not only on its total oxygen content,

but also blood pO_2. It is known that decrease in P_{50} (which reflects a shift of oxyhemoglobin dissociation curve to the left) lowers pO_2 at which oxygen passes from blood to tissue, and this could worsen delivery of oxygen to tissues. The quantitative aspects of this are illustrated in Figures 1 and 2, which show the curves of oxyhemoglobin dissociation in whole blood of rats, solutilns 1 and 2, mixture of solutions and blood. As can be seen in the figures, 50% oxygen bound with hemoglobin in whole blood is released already at pO_2 36 mm Hg; for solution 2 this applies to 21 mm Hg and solution 1, only when blood pO_2 reaches 12.5 mm Hg. One of the most distinct signs of oxygen transport from capillary blood to tissue is drop of mixed venous blood pO_2. Indeed, pO_2 in mixed venous blood was lower, starting at the time of 74% blood substitution, in the 1st group than in the 2d.

Parameters of overall gas exchange and oxygen transport in rats with isovolumic exchange substitution of blood with two solutions of modified hemoglobin

Parameters	Tested group	Baseline data	After substitution of blood			
			45 %	71 %	90 %	[illegible]
Oxygen uptake, mℓ O_2/100 g/min	1	1,31±0,05	1,57±0,07	1,48±0,06	1,15±0,09	0,7 (n = 2)
	2	1,44±0,06	1,59±0,06	1,50±0,08	1,44±0,08	1,40±0,07
CV, mℓ/100 g/min	1	25,9±2,0	37,4±2,6	35,2±3,3	28,3±1,7	16,8 (n = 2)
	2	32,7±3,7	38,5±3.9	52,6±7,2	60,7±6,4	67,0±5,9
Arterial blood O_2 content, vol%	1	15,3±0,8	12,6±0,6	8,7±0,5	7,3±0,4	6,1 (n = 2)
	2	15,8±0,6	11,6±0,5	7,8±0,5	5,4±0,3	5,0±0,3
Mixed venous blood O_2, vol%	1	10,0±0,9	8,4±0,7	5,2±0,6	3,9±0,1	2,7 (n = 2)
	2	11,2±0,9	7,4±0,6	5,0±0,4	3,1±0,3	2,9±0,2
Arteriovenous difference for oxygen, vol%	1	5,3±0,5	4,2±0,5	3,5±0,3	3,4±0,3	3,8 (n = 2)
	2	4,6±0,5	3,9±0,4	2,8±0,3	2,3±0,2	2,1±0,2
O_2 tension in mixed venous blood, mm Hg	1	45,4±2,2	38,5±2,5	27,2±3,7	15,2±1,7	9,3 (n = 2)
	2	46,3±1,3	38,3±2,3	38,7±1,7	28,6±2,9	24,3±1,2

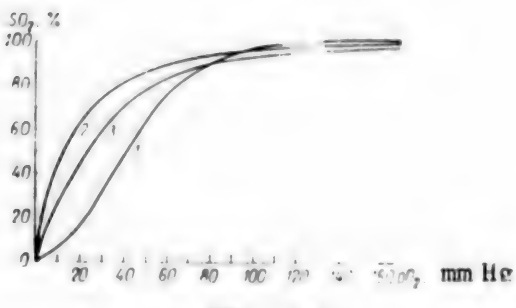

Figure 1.
Curves of dissociation of oxyhemoglobin of whole blood (1) of rats and solutions of modified hemoglobin with high (2) and low (3) affinity for oxygen

In 1980, K. P. Ivanov and Ye. G. Lyabakh [3] performed a detailed mathematical analysis of the quantitative role of various parameters of respiratory function of blood in the transport of oxygen. It was shown that, with moderate and low blood oxygen capacity, P_{50} plays an exceptionally important role in supplying oxygen to tissues. In the present

+ Here and in Figure 2: X-axis, oxygen tension (mm Hg); y-axis, oxygenation of hemoglobin (%)

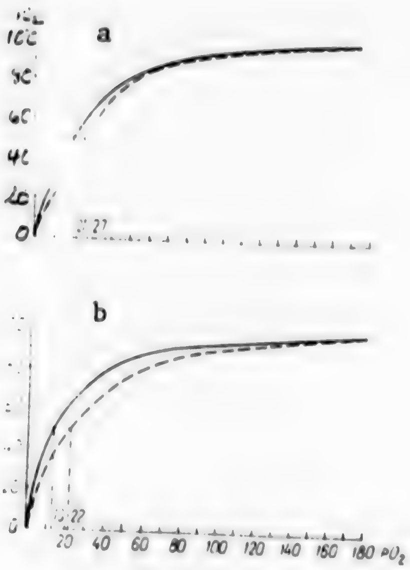

Figure 2.
Oxyhemoglobin dissociation curves for mixture of blood and solutions of modified hemoglobin after partial isovolumic substitution of blood in rats
a) after replacing 74% of the blood with solution 1 (P_{50} 12.5 mm Hg, boldface lines) and solution 2 (P_{50} 21.5 mm Hg, dash lines)
b) after 90% replacement with solution solutions 1 and 2

study, this conclusion was entirely confirmed experimentally for the first time on the example of concrete values: decrease by almost a factor of 2 in oxygen capacity of solution 2, as compared to solution 1, is entirely compensated by a right shift of the oxyhemoglobin dissociation curve of 8.5 mm Hg. These data also have much practical importance. They show the range within which one can retain efficient oxygen-transporting function of blood, compensating for the decline in oxygen capacity with a right shift of the oxyhemoglobin dissociation curve. Of course, this is very interesting to the problem of using oxygen-transporting blood substitutes.

Apparently, another important conclusion is that the poorer delivery of oxygen to tissues with a left shift of the oxyhemoglobin dissociation curve and decline of P_{50} affect primarily the myocardium. The decrease in strength of the myocardium and CV leads to further worsening of oxygen delivery to tissues, as indicated by the decrease in oxygen uptake and dramatic decline of pO_2 in mixed venous blood.

The results of this study make it possible, for the first time, to furnish a quantitative assessment of efficiency of oxygen transport by blood, concurrently for three extremely important physiological parameters: oxygen capacity, blood P_{50} and CV.

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INVESTIGATION OF EFFECT OF SILVER COMPOUNDS ON MICROFLORA IN WATER RECLAIMED FROM ATMOSPHERIC MOISTURE CONDENSATE IN A CLOSED ENVIRONMENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 11 Nov 85) pp 80-82

[Article by M. I. Shikina, Yu. Ye. Sinyak, S. V. Chizhov and N. B. Kolesina]

[English abstract from source] The effect of different silver compounds (silver sulphate, silver nitrate, electrolytic ionic silver) on microorganisms in water reclaimed from the amospheric condensate in an enclosed environment was investigated. The following microorganisms were examined: Alcaligenes faecalis, Citrobacter freundii, Aeromonas hydrophylla, Staphylococcus epidermitis, etc. The ionic silver concentrations in solution varied from 0.1 to 10 mg/ℓ. The efficiency of the silver compounds was found to depend on the microbial strain, ionic silver concentration in solution and time of exposure. The microflora of the reclaimed water proved to be highly resistant to the preservatives which was strongly associated with the bacterial, physical and chemical composition of the products preserved.

[Text] Ions of heavy metals--ionic silver, chlorine- and iodine-containing compounds and others--are among the chemical agents that are used to decontaminate and preserve water. It has been established that the effect of bacterial destruction by silver is attributable to change to an ionic state of soluble metal compounds (Ag_2O, AgCl, AgBr), with the exception of metal compounds of silver sulfide (Ag_2S) formed through interaction with hydrogen sulfide of air [3-5]. The mechanism of action of silver on the bacterial cell involves two stages: the first (reversible) is adsorption of silver by the surface of the bacterial cell and the second (irreversible), combination of bacterial protein with silver ions.

It has been shown that silver ions are bactericidal, not only against vegetative forms of microorganisms (Gram-positive and Gram-negative bacilli, cocci and vibrions), but, in certain concentrations, sarcina, bacteriophages, viruses and sporulated forms of microorganisms [2, 5]. Bactericidal doses of silver ions for vegetative forms of microorganisms range, according to the data of different authors, from 0.05 to 0.5 mg/ℓ, and the effect occurs within 30 min to 1 h [1-5]. According to the data of L. V. Grigoryeva [2], bacteriophage and enteroviruses in water are inactivated 1-5 days after treatment with

silver in concentrations of 0.2-5 mg/ℓ. There are data to the effect that low doses of silver can stimulate growth of microorganisms [5].

The advantage of silver ions is their capacity to retain for a long time their preservative properties, although when water is stored for a long time their concentration drops (by 50-75%) due to adsorption on container walls [4].

It has been established that preservation of potable tap water with silver ions for storage in a closed environment, in a glass container, permits retention of its properties for 3.5 years [6].

It is known that the efficacy of decontaminating water depends on the species of microorganism, salt composition reaction of medium pH and water temperature [4]. Na^+, Ca^{2+} and Mg^{2+} cations have an insignificant effect on the process, while Al^{3+}, Fe^{2+} and Fe^{3+} cations lower significantly the bacteriostatic effect of silver in water due to its adsorption on hydroxides. Anions can be ranked as follows according to their capacity to lower efficacy of silver ions: Cl^-, $>HCO_3$, $>SO_4^{2-}$. Thus, addition to water of 10 mg/ℓ chlorides prolongs disinfection by 25% and 100 mg/ℓ, by 75% [6]. For this reason, one should select the dose of silver to treat water reclaimed from waste or desalinated salt water according to the method of its artificial mineralization and chemistry, as well as quantiative and species-specific composition of microorganisms.

However, the question of selecting effective doses of silver to suppress growth of microflora in water reclaimed from atmospheric condensate, with consideration of its chemical and bacterial composition, requires further work. There are virtually no data in the literature concerning resistance to silver ions of different strains of micrcorganisms and their combinations that are inherent in such moisture-containing proudcts. Few studies have been made of interaction between microflora and preservatives in systems of reclaiming water from atmospheric condensate and other waste, when operating for a long time in a sealed environment. Our objective here was to test the effect of various silver compounds (solutions of ionic silver, silver sulfate and nitrate) in concentrations of 0.1 to 10 mg/ℓ for Ag^+ ion on growth and development of microflora in a condensate of atmospberic moisture and reclaimed water.

Methods

The object of our studies consisted of day-old cultures of microorganisms isolated from atmospheric condensate and reclaimed water during operation of a sorption water-supply system in a closed environment, and humans participated in the experiment. The microorganisms included Alcaligenes faecalis, Staphylococcus epidermidis, Citrobacter freundii, Aeromonas hydrophila and, for comparison, E. coli (strain 675) and Streptococcus faecalis, which are indicator microorganisms in natural potable water. A suspension of each microorganism was prepared separately in pre-autoclaved water. The baseline bacterial burden of suspensions was rather high, constituting 10^4-10^5 microbial bodies/mℓ, which corresponded to their number in samples of water and condensate in the closed environment. In addition, tests were performed with samples of real atmospheric condensate and reclaimed water collected during operation of water-supply systems. Before inoculating samples on nutrient medium (beef-extract agar), the preservative was neutralized with sodium hyposulfite at the rate of

1 mℓ 0.1% solution/ℓ water. The samples were inoculated and colonies counted in the dishes after incubation at 37°C without diluting them (0.1 mℓ samples) and with dilution (1:10, 1:100) using the conventional bacteriological methods.

Results and Discussion

The results of the experiments revealed that the number of viable cells of all species of microorganisms did not change significantly in 4 days (observation time) in untreated control suspensions, and it held at 10^4-10^5 microbial bodies per mℓ. We observed 99.9-100% suppression of bacterial growth under the effect of silver sulfate, starting with a concentration of 0.1 mg/ℓ for silver ions or more. A comparative evaluation revealed that, with 0.1 mg/ℓ silver sulfate, complete inactivation of Alcaligenes faecalis cells in suspension occurred in 1 h, for Citrobacter freundii and Bact. E. coli after 3 h of contact. Streptococcus faecalis and Staphylococcus epidermidis were more resistant to the preservative, and their inactivation with use of the same concentration of silver sulfate occurred only after 24 h. In solutions of silver nitrate in doses of 0.5 mg/ℓ and 1 mg/ℓ for Ag^+ ion, death of all vegetative forms of microorganisms was noted after 4 h, and with a concentration of 10 mg/ℓ, after 10 min. Of the three tested compounds, ionic silver was somewhat more effective as a preservative than silver sulfate and nitrate. However, subsequent tests on samples of real condensate and reclaimed water revealed that 0.1 mg/ℓ ionic silver was not sufficiently effective to completely suppress growth of microflora. In a dosage of 0.1 mg/ℓ preservative, residual growth of microorganisms in the samples constituted 10^2-10^3 microbial bodies/mℓ, which is indicative of their significant resistance under such conditions. With 0.5-1.0, 5.0-10.0 mg/ℓ silver compounds in samples of atmospheric condensate and reclaimed water, complete suppression of microorganism growth was observed after 30-60 min contact with the preservatives. However, continued storage of the samples with preservatives for 3 days failed to reveal reactivation of growth of microorganisms only when silver ions were present in concentrations of 1.0 mg/ℓ or more (Ag_2, SO_4, Ag NO_3), while with use of a solution of electrolytic ionic silver insignification growth in the samples was observed with a concentration of 1 mg/ℓ. In the samples with 0.5 mg/ℓ concentration of Ag^+ ion, residual growth of microorganisms did not exceed 100 microbial bodies/mℓ. Thus, it was shown that the efficacy of silver compounds depends on concentration of silver ions in solution, duration of preservative action and baseline burden and species of microorganisms, which is consistent with the findings of a number of authors [1-6].

Of considerable interest are the data obtained when we checked the results of the laboratory experiments with those obtained from testing operational systems of water purification from atmospheric condensate. For example, after the system had treated 174 ℓ water, considering intermediate storage in a special container for 55 days, no growth of microorganisms in reclaimed water was observed when it contained silver ions in a concentration of 0.6-0.2 mg/ℓ. However, up to $5.7 \cdot 10^3$ microbial bodies/mℓ slipped through in 199 ℓ water, when silver ion concentration in water was 0.44 mg/ℓ. In this time, the water met the standards according to the main hygienic parameters (bichromate oxidizability, nitrogen of nitrates and nitrites). In another experiment, it was shown that bacterial contamination of reclaimed water constituted 1.48-$3.15 \cdot 10^4$ microbial bodies/mℓ, in the presence of 0.02-0.05 mg/ℓ ionic silver in the water at one of the stages of operational testing of an installation in

a closed environment. In some water samples, residual growth of microorganisms constituted $1.2 \cdot 10^3$ microbial bodies/mℓ with silver ions in a concentration of 0.15 mg/ℓ.

Thus, it can be concluded that, in the case of prolonged operation of systems for reclaiming water from atmospheric condensate in a closed environment, particularly when there are interruptions in operation, favorable conditions are created for development in water of strains of microorganisms with rather high resistance to silver ions. This is apparently related to the distinctions of physicochemical and bacterial composition of these moisture-containing products. Probably, we cannot rule out the possibility of microorganism adaptation to silver ions when a preservative is used for a long time. However, this matter requires further investigation.

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METHODS

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DEVELOPMENT OF METHODS FOR THE STUDY OF SPACE MOTION SICKNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 15 Aug 86) pp 83-88

[Article by A. D. Matveyev]

[Text] Current theories on the pathogenesis of space motion sickness (SMS) served as the basis to develop methods for studying and preventing SMS: intralabyrinthine and interanalyzer "conflict" (mismatch of sensory inputs), onset in weightlessness of disturbances referable to dynamics of spinal fluid (due to shift of body fluids in a cranial direction), as well as this author's own conception that development of circulatory static venous ischemia and hypoxia of the brain is the cause of SMS.

We describe briefly below the methods and instruments that have been developed, and submit the results of inflight and ground-based studies of vestibular function and SMS conducted by this author over a 20-year period.

Onboard instrument for testing vestibular analyzer function under spaceflight conditions. Methods of vertical writing (graphic recording of vestibulomotor reactions) and successive visual image were used to objectivize vestibulosensory responses during the vestibular functional test with head movement [3, 12, 32, 45, 55]. The studies using this method were carried out on the 4th day of flight aboard Soyuz-8 in 1969, during technical twisting of the spacecraft. As a result of the studies, significant increase (more than 10-fold) was demonstrated in the vestibulotonic reflex (arm deflecting response), as compared to ground-based data. Alleviation of the motor reaction was indicative of increased sensitivity of the cupuloendolymphatic system to angular (precession) accelerations in the acute period of adaptation to weightlessness (Figure 1).

Onboard instrument for examining visual and vestibular mechanisms of orientation in space and determination of causes of illusions in flight. Methods of visual and tactile-kinesthetic determination of the subjective vertical and horizontal (craft axes) in a field without reference points were used [4, 6, 46, 56, 58]. The studies were conducted during an 18-day mission aboard Soyuz-9 in 1971. The results revealed that, in weightlessness, otolith gravireceptors do not play an appreciable part in formation of visual spatial orientation, as indicated by the insignificant increase in errors in determining spatial

coordinates. One of the demonstrated distinctions in assessing positions of vertical and horizontal coordinates in weightlessness is that the parameters coincided when determining visual and tactile-kinesthetic coordinates. The magnitude of error in both test methods depended on the amount of tactile information (when touching with the feet and without touching), which is indicative of formation of a new functional orientation system in weightlessness. This is associated with increased significance of tactile and proprioceptive analyzers as compensation for change (elimination) of graviceptor function of the otolith system in weightlessness. The tests on the first postflight day revealed a dramatic imbalance in visual and tactile-kinesthetic determination of coordiantes, which was manifested in the form of gross errors (by 40-60°) in subjective determination of spatial coordinates. The results of the studies indicate that the illusions (perigravic) of body position are otolithic in nature; they occur in many cosmonauts with sudden onset of weightlessness (Figure 2).

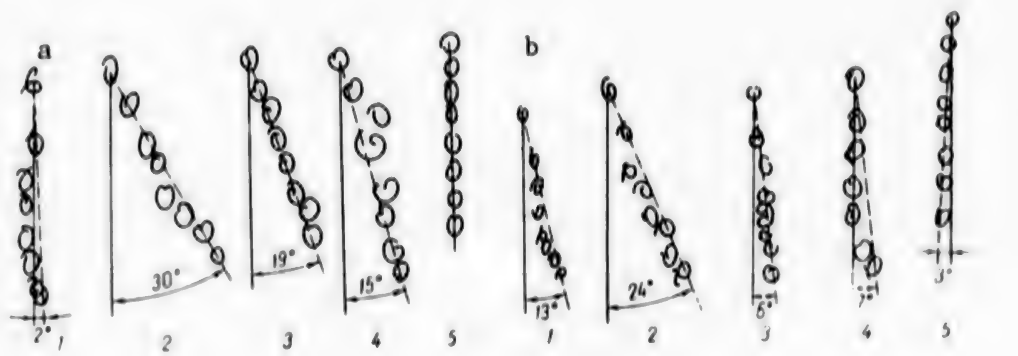

Figure 1. "Vertical writing" test of commander (a) and flight engineer (b)

1-3) inclination to the left, right and forward, respectively
4) eyes shut
5) eyes open

Onboard SMS questionnaire. The questionnaire is intended for special study and comparative evaluation of SMS symptoms and tolerance to spaceflight as related to ground-based determination of vestibulovegetative resistance (VVR) and history of motion sickness (MS) [9, 47, 51], and it consists of two parts: questions which the cosmonauts answer before and after flight, and questions that they answer in written form during the flight. The questionnaire was used during missions of 5 international and 1 Soviet crew aboard Soyuz-37, Soyuz-38, Soyuz-39, Soyuz-40, Soyuz T-6 and Soyuz T-7.

As a result of the studies pursued with use of this questionnaire, additional information was obtained about the incidence, sequence and distinctions of development of SMS symptoms in flight, as well as data referable to qualitative and quantitative evaluation of severity of symptoms in the acute period of adaptation to weightlessness; it was found that appearance of these symptoms is a function of spaceflight conditions and factors, nature of work; the role of individual predisposition of baseline and acquired VVR, role of motor

activity, "rush of blood to the head," optokinetic stimuli and other factors in development of SMS. Data have been obtained concerning development of illusions and their relation to onset of SMS, as well as effects of various preventive agents on SMS symptoms.

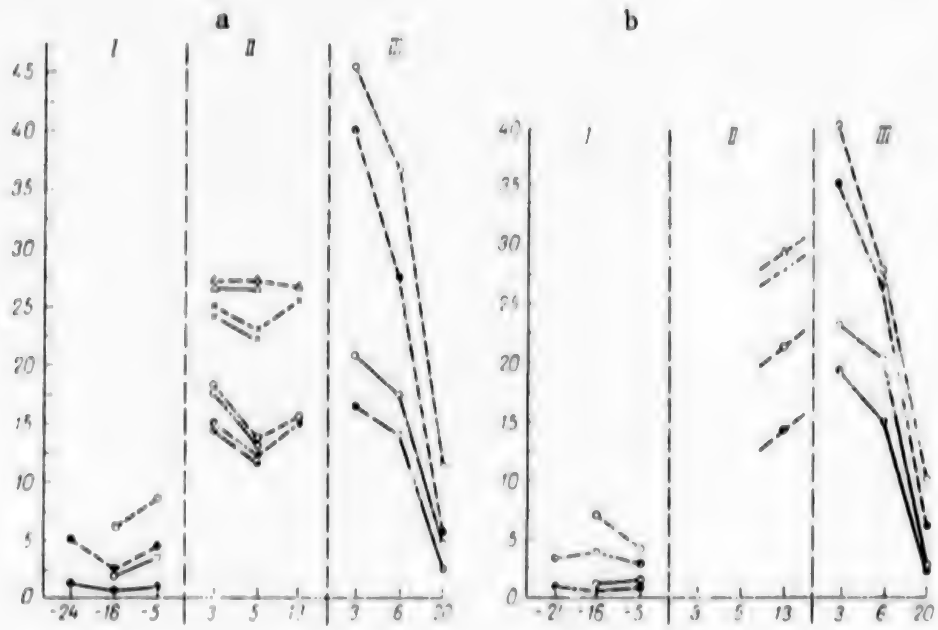

Figure 2. Result of finding the "vertical" by commander (a) and flight engineer (b) by visual (boldface line) and tactile-kinesthetic (dash line) methods

X-axis, day of test; y-axis, deviation (degrees)
I) before flight
II) during flight
III) after flight
●) vertical when standing
○) vertical when recumbent
×, △) the same without immobilization of legs

A set of vestibular parameters was elaborated for onboard electrophysiological equipment, with which a study was made of vestibular function in the course of the acute period of adaptation to weightlessness according to nature of oculomotor reaction during the flight of Soyuz T-7 in 1982, in order to determine the role of the vestibular system in development of SMS. The method consisted of a functional test, the head moving in a frontal plane, with recording of oculomotor reaction by means of onboard equipment. As a result of comparising ground-based (before and after flight) and flight tests, which was done together with G. I. Gorgiladze for the first 4 flight days, a differentiated nature of changes was demonstrated in otolith function in weightlessness. Analysis of electrooculograms revealed that there was disappearance of the compensatory otolith reaction of counterrotation of the eyeball and appearance of a nystagmoid reaction, which was indicative of depression of

gravirecepter function of the otolith system and increase in its sensitivity to inertial stimuli during head movement [2, 43, 52, 54].

Instrument for testing threshold sensitivity and reactivity of vestibular analyser. Methods of caloric (temperature) stimulation were used. The distinction of such a method is the contact method of cooling or warming the labyrinth by means of a semiconductor thermoelectric battery, by varying temperature (from 2 to 47°C) in an ear probe inserted in the external auditory meatus [25, 58]. As a result of the studies, data were obtained which permitted qualitative and quantitative evaluation of excitability of the human vestibular analyzer. The advantage of this method is that it is possible to determine precisely, maintain and measure a fixed labyrinth temperature throughout the test period with the head in any position.

Instrument for testing excitability of vestibular system. This is a method of stimulating the labyrinths with graded direct or pulsed current [10, 37, 50]. The parameters of the instrument permit delivery of afferent (subliminal), threshold electrostimulation of the vestibular system. Using the method of bipolar equal stimulation, it was possible to attenuate and suppress vestibulomotor and sensory responses (nystagmus and illusions) with threshold levels of current. The results of studies have shown that it is possible to effect electrophysiological control of the functional state of the vestibular system and affect undesirable reactions.

Electric rotating vestibulometric unit. It is intended for adequate stimulation of the vestibular system with anbular and linear accelerations in order to test threshold sensitivity and reactivity (cupulometry) of the vestibular analyzer, demonstrate distinctions of interaction between the cupular and otolith systems and vestibular asymmetry during sinusoidal rotation. Special functional tests were developed for these investigations: "otolith cupulometry"--during rotation with the head in central and eccentric position, and "otolith response with squatting" (expanded technique to examine otolith function, the OR test). As a result of laboratory sutdies, data were obtained on interaction between the otolith and cupular systems (enhancement or attenuation of otolith responses as a function of start of simultaneous stimulation of the cupoloendothelial system) [29, 38, 43].

For ground-based investigation of the pathogenesis of MS, equilibrium and spatial orientation, as well as to study the biomechanics of human movements under conditions of unstable equilibrium and simulation of absence of static load, a device was developed that consists of an unstable support with three degrees of freedom, effect of space without static load and increased inertia, which were produced by means of a half-sphere with the apex and point surface of the support directed down. The unit provides for automatic regulation of the position of the general center of gravity. The method involves active and passive balancing, as well as rotation in the horizontal plane about the vertical axis of the unit, which may or may not coincide with the gravity vertical.

Unit for examining patients with functional vestibular disorder [11, 13, 15, 44]. This is a unit that consists of a table for immobilization of the patient, which is secured in the inside frame of a gimbal which rotates on half-axes

in an external cradle placed on a support. The turns of each cradle about the vertical and horizontal axes (by an angle of ±360°) and their fixation with 1° margin of error are effected by menas of a planetary and worm gear mechanisms, respectively, by the manual controls. The outside and inside frames have units to control the individual's position on three axes and to attach the helmet with the head immobilized on it, on the inside and outside frames. A commutation block for connection of electrophysiological equipment is installed on the stationary base of the stand. With the subject immobilized in a position of physiological rest on the table, tests are performed for positional nystagmus, placement nystagmus and neck nystagmus under standard conditions of functional tests with passive changes in position in the form of successive inclination of the body and head as follows: forward, back, to the right, to the left, to 60° and in antiorthostatic position (-10° angle) with each bend. The changes in position are made at different speeds: at the rate of 1°/s for testing positional and cervical nystagmus and 10°/s for testing placement nystagmus.

Unit for testing excitability of vestibular analyzer. The method of air calorization of the labyrinths was used in the studies [46, 49, 59]. The base of the device consists of the assembly of semiconductor theroelectric batteries, which produce a temperature gradient of 2 to 52°C for the flow of air passing through them as a function of polarity and level of voltage. The device provides for rapid achievement of set temperature, stability of temperature of air flow, as well as precise monitoring and control of velocity, pressure and volume of air delivered to the external auditory meatus. The design of the ear probe-tubes permits testing of caloric reactions of both animals and man. The results of laboratory studies revealed a number of distinctive features in vestibular reactions and advantages of the method of air calorization of the labyrinths over calorization of water: longer latency period of responses, slower build-up and extinction of reactions. Although motor and sensory reactions (nystagmus and illusions) may reach the same intensity with air calorization of the vestibular system as with calorization of water, subjectively the caloric test using cool or warm air is tolerated better. The autonomic reactions are less marked. We must mention the total safety of the air caloric test, regardless of condition of the outer and middle ear.

On the basis of analysis of the results of our own ground-based and inflight studies, as well as data in the literature, new ways and means have been developed for prevention and elimination of SMS, that direct themselves to different elements of the pathophysiological mechanism of SMS.

Device that provides graded and controllable application of force to the occipitocervical antigravity muscle group and simulates application of weight to the cervical spine by means of symmetrical pairs of forces, as well as decrease in stimulation of vestibular system by angular accelerations by means of restricting head movement. The magnitude of the load was calculated with consideration of average weight of the head on the ground, which constitutes 7% of body weight, position of the head's center of gravity which is to the front of the occipitocervical articular, and mean distance from the articulation axis to the region of attachment of occipitocervical muscles (Figure 3). The method of therapeutic and preventive use of the device involves wearing it at work, constantly or periodically for the first 3-4 days of the

acute period of adaptation to weightlessness. The load is determined individually, ranging from higher to lower values. The device can also be worn at night in order to normalize sleep, restore body schema and provide psychological comfort.

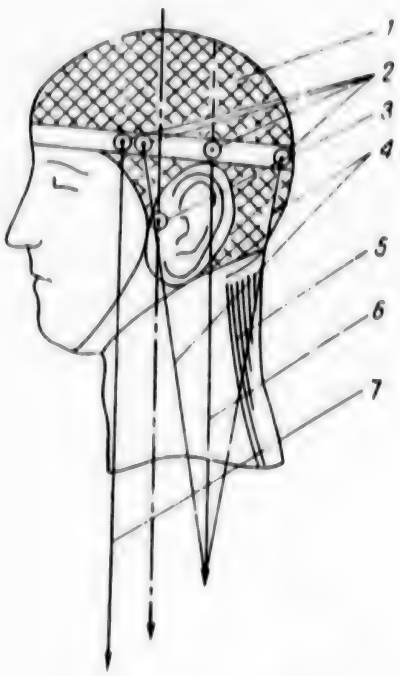

Figure 3.
Drawing of load produced by means of device for prevention and elimination of SMS in flight
1) head mass
2) points of application of load
3) head's center of gravity
4) vector of force of restricting head movement
5) occipitocervical antigravity muscles
6) vector of force applied to cervical spine (along axial line of supporting occipitocervical articulation)
7) vector of force applied to occipitocervical antigravity muscles

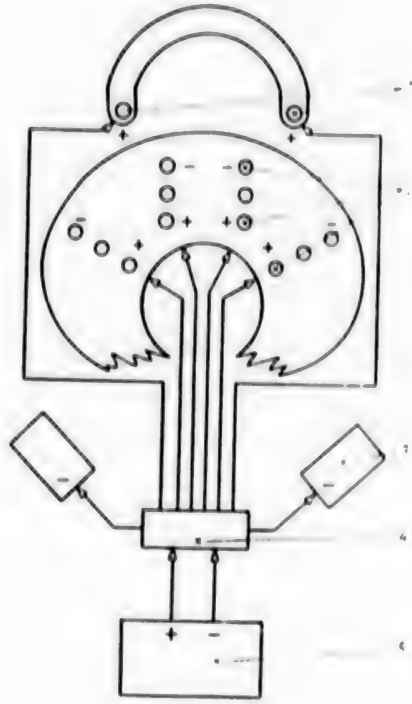

Figure 4.
Drawing of arrangement of electrodes for stimulation of cervical antigravity muscles
1) labyrinthine electrodes
2) cervical electrodes
3) passive electrodes
4) commutation block
5) power source

The efficacy of this device as a means of suppressing vertigo, illusions, discomfort and nausea was noted as a result of its use during flights of Soyuz T-3, Soyuz-39 and Soyuz-40 spacecraft with the Salyut-6 orbital station, and that of Soyuz T-7 with Salyut-7 orbital station. The cosmonauts reported that wearing the device improved their general condition and did not hinder their work. It did not elicit undesirable side-effects, and for this reason can be used without restrictions during flights [55].

The elicited protective effect of suppressing sensory and autonomic responses is based on the principle of simultaneous action on several pathogenetic mechanisms at the early stage of development of SMS. This is achieved by the following physiological mechanisms: normalization of the system of vestibulo-cervical reflex which provides the *vestibulovisual mechanism* (cristo-ocular, maculo-ocular and cervical reflexes) of stabilizing the field of vision when the head is moved, and *vestibulocervical proprioceptive* mechanism when orienting the position of the head in space; regulation via a vestibular mechanism (canal-otolith signaling) by means of restricting the range and velocity of head movements; action of a tactile mechanism related to stimulation of reflexogenic zone of the parietal region of the head, which has high sensitivity to weightlessness.

Method of multichannel controllable electrostimulation of the posterior antigravity group of cervicle muscles. Studies were pursued using an onboard instrument, an electric stimulator, with use of bipolar electrodes of pulsed and alternating sinusoid current, the parameters of which provide for sufficient signal power (no more than 50 mW) [8, 18, 19, 35, 39]. Use of electric stimulation at subliminal levels of above current has a tonic effect on cervical antigravity muscles, it does not elicit discomfort or pain, fatigue, and it is safe to use. The method can be used together with electrostimulation of antigravity muscles of the body (back, legs) or with concurrent afferent equal anodal electrostimulation of labyrinths with pulsed current (Figure 4). The results of testing the method under laboratory conditions revealed its validity and efficacy in preventing and suppressing autonomic vestibular symptoms of SMS without any side-effects.

Analysis of previously published clinical and experimental data [14, 20, 22, 23, 26, 28, 30] and results of this author's investigation (in collaboration with Ye. A. Kovalenko) made it possible to validate the conception of pathogenesis of motion sickness as a result of development of cerebral hypoxia. According to this conception, under ground-based conditions development of MS on the basis of cumulative stimulation of the vestibular system appears as a result of impaired vascular regulation of the brain with change in vascular tonus (in the system of the internal carotid and vertebral arteries), which causes local hemodynamic disturbances in the brain and some degree of hypoxia in different parts of the brain. Our investigations with simulation of MS revealed a 30-50% drop of blood PO_2 in the head with onset of the nausea-vomiting reflex of MS.

According to the expounded conception, the mechanism of development of SMS is also based on cerebral hypoxia due to the change in systemic and cerebral hemodynamics in weightlessness [5, 16, 17], with development of circulatory static venous ischemia of the brain [7, 24, 42]. Stimulation of the vestibular system against such a background enhances cerebral hypoxia, induces MS and aggravates its course. From the standpoint of pathogenesis, we can explain the contribution of PO_2 to the overall mechanism of development of motion sickness, in which acute vestibulovegetative dysfunction arises in the presence of disorders of vascular mechanisms of intracranial circulation and diminished oxygenation of the brain. However, special investigations are required to assess the independent role of measuring blood PO_2 in the pathogenesis of ground-based MS and SMS.

A combined method of pathogenetic prevention and elimination of MS under laboratory conditions was elaborated on the basis of the conceptions of pathogenesis of MS that are being developed, and it has been tested successfully; it involves periodic, brief breathing of gases and hyperoxic-hypercapnic gas mixtures combined with intake of pharmacological agents. This achieves a differentiated effect simultaneously on several elements of the mechanism of the early stage of development of this condition: it blocks cholinoreceptors, has a tonic effect on the central nervous system, a sedative effect on mental functions and normalization of the main bioenergetic process--biological oxidation in the brain. This combined method normalizes the basic body functions, enhances resistance, diminishes fatigue and, consequently, improves work capacity.

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BRIEF REPORTS

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INVESTIGATION OF ENERGY METABOLISM OF BIOLOGICAL SYSTEMS IN WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 28 Feb 86) pp 89-90

[Article by M. G. Tairbekov]

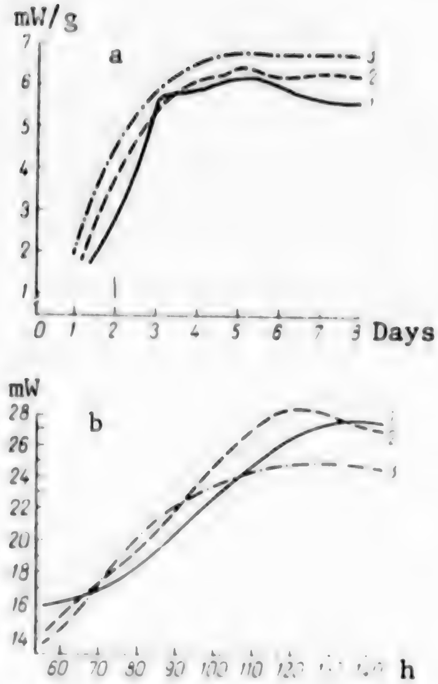
[Text] On the basis of analysis of data in the literature and results of our own studies, it could be assumed that there should be less than normal energy expenditure by biological systems (in particular, cells) in weightlessness. Such a decline in expended energy could be expected primarily due to diminished energy used to maintain mechanical strength of the system. It was interesting to examine the dynamics and intensity of energy metabolism in microgravity.

Methods

Two experiments were conducted, using the Biocalorimeter instrument [1], in weightlessness: aboard Cosmos-1514 (13-19 December 1983) and Cosmos-1667 (10-17 July 1985) biosatellites. Germinating corn seeds and developing drosophila pupae, respectively, were the objects of our studies.

The time at which the instrument was filled with biological material and the biocalorimeter was placed aboard the biosatellite in the flight experiment and in a mock-up of the biosatellite in ground-based control studies was considered to be the start of the experiment (0 day). Measurements were begun 14-16 h after the instrument began to function in the working mode and temperature was stabilized in the instrument. Throughout the experimental period, the output signal from the instrument was measured automatically every 2 h, just prior to flushing the working and control chambers with air. The magnitude of the signal was recorded by the recording device and relayed to earth via telemetry channels. Thus, we were able to observe the dynamics of increasing generation of heat corresponding to dynamics of energy expended in the course of the flight experiment and control studies. In processing the results obtained in flight and control experiments, the amount of heat generated as a whole from all seedlings or pupae was scaled to 1 g weight of initial material and expressed in milliwatts.

Since the seeds sprouted in the dark, which ruled out photosynthesis, during development of seedlings there was only transformation of endosperm reserve



Dynamics of heat release by sprouting corn seeds (a) and developing drosophila pupae (b) in weightlessness
Y-axis, amount of heat released (mW); x-axis, days (a) and hours (b) of experiment
1) flight
2) control in mock-up
3) laboratory control

substances into structured organ tissues, the biomass remaining relatively constant. In insects, at the pupal stage there is lysis of temporary organs and tissues, followed by histogenesis that is coordinated with morphogenetic movement of cells, and biomass is unchanged.

Postflight analysis involved calculation of heat generated within specific intervals.

Results and Discussion

The results of our studies are illustrated in graphic form in the figure. As can be seen from the plots, all of the curves of dynamics of heat generation in flight and control experiments had the same configuration and correspond to the universal biological curve with a sigmoid shape. Each of the segments of these curves characterize the time period of heat release corresponding to specific phases of development of the biological systems under study: first period of development--period of intensive development; phase of slower development and stationary phase. It is apparent from this that the changes in metabolic activity of sprouting corn seeds and developing drosophila pupae corresponding to specific phases of development are identical in weightlessness and in earth's gravity. However, a comparison of the main segments of the curves reflecting intensity of energy expenditure shows that it is lower when the tested biological systems developed in weightlessness than in the ground-based experiments. Nevertheless, mathematical processing of the data failed to demonstrate reliable differences between experimental and control variants. This means that conditions associated with weightlessness did not affect the level of basal energy metabolism in plants and insects when using the energy of chemical bonds for division, growth and differentiation of cells.

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DIFFERENTIATION OF HEMOPOIETIC STEM CELLS DURING ADAPTATION TO HIGH ALTITUDE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (manuscript received 18 Mar 86) pp 90-91

[Article by O. I. Andreyeva, V. V. Pukhov and S. B. Daniyarov]

[Text] It is known that exposure of a biological system to a hypoxic environment leads to stimulation of erythropoiesis and increase in number of red cells in peripheral blood. At the same time, no studies have been made of the distinctions of differentiation of hemopoietic stem cells (HSC) during the period of adaptation to high altitude. Nor is there clarity as to the level (stem or committed cells) on which mountain hypoxia alters the direction of differentiation. Our objective here was to investigate the distinctions of HSC differentiation during the period of adaptation to high altitude.

Methods

Experiments were performed on 156 CBA mice weighing 22-25 g. The direction of differentiation of HSC was studied by the method of spleen exocolonies [5]. Mice adapted to high-altitude (Tuya-Ashu mountains, 3200 m) served as donors. The donor mice were sacrificed on the 3d, 7th, 14th and 30th days of adaptation, and bone marrow was flushed from their femurs. A suspension of bone marrow ($4 \cdot 10^4$ karyocytes) was injected into the caudal vein of recipient mice. CBA mice, which had been exposed to a lethal dose of radiation (^{137}Cs γ-radiation, 10.0 Gy or 258 mCi/kg dose) just before the bone marrow injection, served as recipients. One recipient was given bone marrow from five donors. The recipients were sacrificed on the 8th day after giving them bone marrow, the spleen was fixed in Bouin solution and sections 4 μm thick were prepared then stained with hematoxylin and eosin [3]. Differentiation of HSC was evaluated by counting the different types of hemopoietic microcolonies on three sections from each spleen. We used 8-10 recipients at each stage of adaptation. Red and white blood cells were counted in blood of mice at different stages of adaptation to high altitude. Parameters obtained in a valley (city of Frunze, 760 m) served as a control.

Results and Discussion

The results of our study revealed that in a normoxic environment (valley) HSC differentiated primarily in cells of the granulocyte class. Fewer erythroid

and megakaryocyte colonies were demonstrable, and even less mixed ones (see Table). Exposure of mice to mountain hypoxia altered the direction of differentiation dramatically. Thus, already on the 3d day of adaptation there was a decrease in number of erythroid and megakaryocyte colonies and almost 5-fold increase in percentage of mixed colonies. At subsequent stages of adaptation, this pattern persisted: the share of erythroid colonies diminished (particularly on the 30th day), the number of mixed colonies remained high, there were fewer megakaryocyte colonies than in the control, while the number of granulocyte colonies did not change appreciably. Considering such a nature of differentiation, we can explain the significant decrease in number of eoxgenous colonies on the surface of the spleen during the adaptation period (when bone marrow was stimulated by hypoxia), since macroscopic counts revealed mainly erythroid colonies [4]. Microscopic evaluation of intensity of colony formation revealed that considerably more microcolonies are formed in the adaptation period than in the valley; they are diffuse and cannot be counted, and there is prevalence of mixed colonies. It is difficult to explain the appearance of a large number of mixed-type colonies. This is probably due to the influence of the stromal microenvironment [2], since recipient mice were also in a hypoxic environment.

Differentiation of HSC in spleen of irradiated recipient mice, and dynamics of formed elements of mouse blood during period of altitude adaptation (M±m)

Hemopoietic colonies	Control (valley)	Day of high-altitude adaptation			
		3	7	11	30
Erythroid, %	30±8	19±5	14±3	11±3	6±2*
Granulocyte, %	37±9	29±5	30±3	32±5	37±4
Megakaryocyte, %	23±5	4±2*	8±3*	6±2*	15±3
Mixed, %	10±2	48±6*	48±7*	50±10*	42±5*
Number of colonies on spleen surface	21±4,6	8±0,8*	18±2,2	8±1,4	10±1,3
Erythrocytes, million/μℓ	6,1±0,2	6,9±0,3	7,0±0,4	7,2±0,4*	8,3±0,2*
Leukocytes, thou/μℓ	3,50±0,28	3,07±0,42	3,88±0,44	4,0±0,3	3,01±0,24

* $p < 0,05$ as compared to control.

The decrease in share of erythroid colonies in the altitude adaptation period, against the background of increase in blood erythrocyte count, enables us to conclude that erythropoietic affects committed precursor cells rather than hemopoietic stem cells. Less intensive formation of colonies of the megakaryocyte type than in the valley is probably due to diminished platelet requirements, since hypocoagulation changes develop in the adaptation period [1].

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CURRENT EVENTS AND INFORMATION

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THIRD SOVIET-FRENCH SYMPOSIUM ON SPACE CYTOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (signed to press 13 Apr 87) pp 92-95

[Article by I. B. Krasnov]

[Text] The Third Soviet-French Symposium on Space Cytology, which was organized within the framework of collaboration in the area of medicine and medical technology between the USSR Ministry of Health and French National Institute of Health and Medical Research, convened from 4 through 11 May 1986 in France, in the city of Reims. The first such symposium on space cytology convened in Paris in 1983 and the second, in Moscow in 1984.

Space cytology is a discipline that studies the effect of spaceflight factors (weightlessness, high-energy particles, etc.) on the structure, function and metabolism of prokaryote and eykaryote cells (of bacteria, plants, animals). In view of the intense exploration of space, increase in duration of manned orbital station missions, investigations in the field of space cytology are acquiring increasing significance to the solution of both theoretical and practical problems of space biology and medicine. Space cytology acquired fundamental material concerning the effects of spaceflight conditions on the cell as a result of experiments performed aboard biosatellites, spacecraft and orbital stations. At the same time, further development of methods of quantitative cytochemistry, immunocytochemistry and electron microscope stereology offer new opportunities for the study of cells of bacteria, plants and animals that have flown in space.

The symposium program consisted of 7 meetings (the 1st was plenary, the 2d convened under the title of "Nerve Cell," the 3d under the title of "Lymphocytes and Cells in Tissue Cultures," the 4th--"Bone Tissue," the 5th--"Erythrocyte," 6th--"Analytical Methods," 7th--Biological Models") at which 22 papers were delivered.

At the plenary meeting, the paper of M. Bouteille on the subject of "Current Problems of Cell Biology as Related to Investigation of Effects of Space Environment" (Institute of Biomedical Research, P. and M. Curie University, Paris) dealt with general problems confronting space cytology. It discussed experiments dealing with cell biology, which were carried out by French specialists aboard a spacecraft on the program of the European Space Agency.

A survey paper by I. B. Krasnov, "Advances in Soviet Space Cytology" (Institute of Biomedical Problems, Moscow) submitted the results of cytological studies pursued in the Soviet Union of the effects of microgravity on metabolism, structure and function of cells of fungi, tissue cultures, various rat organs and tissues flowin in space aboard biological satellites of the Cosmos series.

A series of papers reflected the urgen need, which has arisen in recent times, of expanding neuromorphological studies of animals exposed to weightlessness. The paper of I. B. Krasnov, "Quantitative Cytochemical Analysis and Its Possible Use in Space Cytology" (Institute of Biomedical Problems, Moscow) described metnods developed by the author for quantiative cytochemical and histochemical analysis of enzyme activity in individual isolated neurons and structures of the brain, as well as the results of using these methods to study the brain of rats flown in space aboard the Cosmos series biosatellites. Changes were demonstrated in vestibular structures of the brain elicited by earth's gravity effects on the otolith system after animals were exposed to weightlessness.

Adaptation to weightlessness is associated with reorganization of the system of interneuronal contacts in the cerebral cortex, as shown in the paper of L. N. Dyachkova, "Ultrastructural Bases of Adaptive Processes in the Brain of Animals Exposed to Altered Gravity" (Institute of Evolutionary Morphology and Ecology of Animals, USSR Academy of Sciences, Moscow). Along with destructive changes in some axodendrite synapses, indicative of loss of functional activity, complex synaptic complexes in different layers of the somatosensory, visual and olfactory cortex of rats flown for 7 days in space aboard Cosmos-1667 showed appearance of growth hillocks and new synapses at different formative stages, which is indicative of a process of de novo formation of synaptic connections.

The paper of G. Geraud, C. Masson, A.-M. Dupuy-Coin and M. Bouteille, "Purkinje-3 Experiment: Preliminary Results of Morphometric Analysis" (Institute of Biomedical Research, P. and M. Curie University, Paris), submitted data obtained by the authors in the Purkinje-3 Soviet-French Experiment, which was conducted on the program of rat experiments aboard Cosmos-1667. The results of morphometric analysis of glomerules in the cortex of the central lobe of the vermis cerebelli of rats flown in space for 7 days confirmed the fact that there is increase in volume of glomerules in the same structure, which the authors had previously discovered in the Purkinje-1 Soviet-French experiment, which was conducted within the framework of an embryological experiment with rats aboard Cosmos-1514. The increase in volume of glomerules, in which one finds the endings of moss fibers that carry proprioceptive impulsation from proprioceptors of muscles, tendons and interarticular surfaces of the posterior extremities, is apparently indicative of an increased flow of impulsation from rat proprioceptors under the effect of earth's gravity following weightlessness.

A. Privat (Institute of Biology, Montpelier), in a paper entitled "Purkinje-2 Experiment: Culture of Rat Embryo Cerebellum," delivered jointly with I. V. Viktorov (Brain Institute, All-Union Mental Health Research Center, USSR Academy of Medical Sciences), and J. Drian, submitted the results of the joint Soviet-French Purkinje-2 experiment, conducted within the framework of

the embryological experiment with rats aboard Cosmos-1514. Electron microscopy of neurons in postflight cerebellum cultures from rat embryos that developed in weightlessness from the 13th to 18th day of prenatal ontogenesis, failed to demonstrate any changes in neuronal ultrastructure and, in the opinion of the authors, was indicative of absence of effect of microgravity on the genetically determined capacity of cerebellar cells to effect growth and differentiation processes.

A parallel between the condition of ultrastructure of lymphocytes, which are normal killers, and decline in their functional activity has been established in man during long-term spaceflights. As shown by I. V. Konstantinov in his paper, "Ultrastructure and Function of Lymphoid Antiviral Cells Under Conditions of Microgravity and Hypokinesia" (Institute of Biomedical Problems, Moscow), which was delivered at the meeting on "Lymphocytes and Cells of Tissue Culture," the decrease in cytological activity of normal killers, as demonstrated by the immunological method in man following a 75-day spaceflight, is associated with disappearance of the capacity these cells had of adsorption and spreading on target cells. In the cytoplasm of such normal killers, there is decrease in number of microtubules and microfilaments, there is change in intracellular orientation of Golgi's complex and secretory granules. In human studies conducted on the Soviet-French Cytotox program, following 120-day antiorthostatic [head-down tilt] hypokinesia, a decrease in cytotoxic activity of normal killers and change in their ultrastructure.

C. Beaure d'Augeres, J. Bureau, J. Arnoult, A.-M. Dupuy-Coin and M. Bouteille (Institute of Biomedical Research, P. and M. Curie University, Paris), in their paper "Plasma Cell Experiemnt: Preliminary Results," submitted the results of an experiment conducted aboard a spacecraft in 1985 on the program of the European Space Agency. The authors investigated the effect of weightlessness on hybridoma AM-2 cells, production of antibodies by the hybridoma, ultrastructural and spatial organization of cells, intensity of RNA biosynthesis (autoradiography analysis of ^{3}H-uridine incorporation on semi-thin sections) and amino acid release into the incubation medium. During the spaceflight, part of the cultures were in the onboard centrifuge and exposed to 1 G. Cultures of hybridomas that were exposed on earth to 1 and 1.4 G served as a control. Moderate decrease in number of living cells was found after the flight, and a more significant decline after exposure to hypergravity (1.4 G). RNA synthesis diminished the most in weightlessness.

In the paper of C. Boucheix, "Technique for Identification of Monoclonal Antibodies in Hybridoma Culture" (Brousse Hospital, Villejuif), a method was described for recovery and culturing of antibody-producing cells of AM-2 hybridoma obtained from hybridization of cells of murine myeloma and splenocytes of mice immunized with retinal antigen, used by French specialists in the Plasma Cell experiment aboard a spacecraft. The author described in detail the method of demonstrating monoclonal antibodies in supernatants of hybridoma AM-2 cultures.

At the Bone Tissue meeting, A. T. Lesnyak (Institute of Biomedical Problems, Moscow), in a paper entitled "Interaction of Osteoclast-Activating Factor and Osteoclasts in Simulated Spaceflight," demonstrated that there is coincidence of time of increased production of osteoclast-activating factor by

immunocompetent cells, demonstrated in man during 120-day antiorthostatic hypokinesia, with the time of increase in resorbtive activity of osteoclasts in a biopsy of the iliac bone, which is indicative of the possible role of the immunity system in activation of the resorption process in bone tissue. The expounded hypothesis is supported by the fact that there was increased production of osteoclast-activating factor by rat splenocytes following 40-day antiorthostatic hypokinesia. The author advanced the hypothesis that there is activation in weightlessness of the immunological element of regulation of the process of resorption in bone.

The paper of J.-R. Nefussi, "Model of Bone Formation in Vitro" (University 7, Paris), dealth with the author's development of an original model of osteosynthesis in vitro using osteoblasts of flat cranial bones of the mouse embryo. The model permits cytological analysis of the process of bone formation and its mineralization, as well as to investigate the effects of various factors and pharmacological agents that control these processes, study the effect of weightlessness on formation and mineralization of bone. Formation of segments of bone tissue occurs in culture on the 7th-8th day of culturing. Evidence is submitted of analogy of the areas of bone mineralization in culture to animal bone. Maximum observation of culture growth lasted 21 days.

The mechanisms of interaction between proteins and hydroxyapatite crystals in the course of bone mineralization were discussed in the paper of G. Daculsi, "Protein-Crystal Interaction in Processes of Formation and Growth of Crystals and Phases of Mineralization of Calcified Tissues, and During Calcification" (Odontology Department, INSERM, Nantes). A model was proposed of interaction between the protein and mineral components, according to which bone tissue proteins have specific areas that are necessary for initiation of the mineralization process. Thereafter, proteins determine the direction of mineralization, size and structure of minerals, and the actual mineralization process. The paper discussed the properties of various bone proteins (collagen, enamelin, fibronectin, osteocalcin) and their role at different stages of the mineralization process. It is stressed that protein and mineral components of bone can be submitted to analysis under an electron microscope following animal spaceflights.

The paper of P. Birembaut and J. J. Adnet, "Morphology of the Extracellular Matrix" (Maison Blanche Hospitla, Reims), submits the results of immunohistochemical examination of proteins of interstitial substance of bone, in particular fibronectin, which is of considerable interest because of its involvement in reactions of immune system cells in the presence of pathological processes.

At the session entitled "Erythrocyte," significant attention was devoted to discussion of function, metabolism and structure of erythrocytes of man and animals submitted to long-term antiorthostatic hypokinesia, which permitted reproduction, to some extent, of the circulatory and hematological phenomena associated with weightlessness. In the paper of V. I. Lobachik, A. S. Ushakov and S. M. Ivanova, "Investigation of Function, Structure and Metabolism of Red Blood Cells of Hypokinetic Man and Animals" (Institute of Biomedical Problems, Moscow), it was proven that there are phasic changes in volumes of

blood, plasma, packed erythrocytes, hemoglobin, intensity of glycolytic processes and red cell resistance in the course of 120- and 182-day antiorthostatic hypokinesia in man. In rats, a decline of erythropoietic titer in plasma and depression of biosynthetic processes in bone marrow cell were found after 60-day hypokinesia. Several of the papers at this meeting pertained to methodological aspects of studying erythrocytes. Thus, use of methods with ^{51}Cr to study the life span of red cells, use of ^{59}Fe to study erythropoiesis with the use of a low-background chamber, as well as an attempt to use mathematical modeling of circulatory processes, were demonstrated in the report of J. Valeyre, "Problems of Measuring Mass of Blood and Red Cells" (Hospital Cancer Control Centedr, Reims). G. Potron (Debre Hospital, Reims), in a paper entitled "Rheological Studies in Hematology," described extensive analysis of methods of studying the structure of erythrocytes, as well as hematocrit and rheological properties of blood, such as viscosity and flow. Treatment of a red cell with aqueous solutions of varhing osmolarity and passing erythrocytes through pores (up to 5 μm in diameter) in a metal or teflon filter were proposed to assess the structure of an erythrocyte. Human blood acquires optimum rheological properties with a hematocrit of 35.9; however, this conclusion applies only to bedrest conditions.

At the meeting entitled "Analytical Methods," much interest was inspired by the paper of J. Bisconte, "Analysis of Images of Cell Cultures" (Biocom Society, Les Ulis) at which he demonstrated the capabilities of new equipment for scanning microvideofilming of tissue culture cells. The equipment is small in size and wieght, it operates automatically and permits recording the image of cell cultures on tape in the form of a digital print-out. It can be manufactured in a variant that is suitable for installation in an orbital space station in order to investigate the effect of weightlessness on tissue culture cells.

P. Bonhomme (Reims University) described the results of a search for optimum conditions for studying biological objects under an electron microscope in a paper entitled "Latest Methods of Electron Microscopy." It is suggested that the electron beam, exposure and thickness of sections be reduced, as well as that sections be placed on grids without a tray and that specimens to be viewed under the microscope be cooled, in order to improve integrity of cell structures in ultrafine tissue sections in the course of their examination under an electron microscope.

A method of spatial reconstruction of ultrastructural organization of the cell by means of computer processing of images of cell ultrastructure obtained in electron microscopy, proposed by Y. Epelboin (P. and M. Curie University, Paris) in a paper entitled "Three-Dimensional Reconstruction of Biological Objects," is quite promising for analysis of intercellular interactions. On examples of analysis of various biological objects, the results of a search for means of improving accuracy and informativeness of the method were submitted. It was shown that three-dimensional reconstruction of cell ultrastructure can be used to study interaction of cytotoxic lymphocytes with a target cell in the presence of altered gravity.

At the meeting entitled "Biological Model," the papers of J. Soyer (P. and M. Curie University, Paris, Bajol-sur-Mer), "Sensitivity to Gravity of Marine

Animals" and C. Delettrez, P. Duie, M. Bouteille (MATRA Society, Velizy), "A living Model for the Study of Cell Sensitivity to Gravity," showed that the Convolutida roscofentia marine worm, which inhabits the shores of Brittany, can be used as an object for the study of effects of microgravity. The advantages of this worm are that it is small (body length 4 mm), symbiosis with algae provides regeneration of oxygen in the environment when a tank is illuminated, the worm reacts to change in gravity by changing its position in space, it can be fixed rapidly for electron microscopy and cytochemical examination of the statocyst, statolith and neurons that receive impulsation from the statocyst. An animated discussion was inspired by the paper of J. Bureau, G. Geraud and M. Bouteille (P. and M. Curie Institute, Paris), delivered jointly with W. Briegleb (Institute of Aviation Medicine, Cologne, FRG), "Cellular Model of Exposure to Hypergravity and Simulation of Hypogravity," which reflected an attempt at determining the dependence of rate of cell proliferation on gravity. According to the data of these authors, hybridoma AM-2 cells proliferated more slowly by a factor of 3.5 when exposed to 2, 4, 6 and 8 G than at earth's gravity. At the same time, exposure to hypogravity in a clinostat also led to transient slowing of cell growth rate.

We should comment on the high scientific and organizational level of the symposium. The results of experimental studies submitted there are a substantial contribution to development of our conceptions of the effects of altered gravity, in particular weightlessness, on the structure, metabolism and function of human and animal cells.

This symposium demonstrated the successful development of Soviet-French collaboration in space cytology, the fruitfulness of joint research, the results of which are very important to the solution of theoretical and practical problems facing space biology and medicine.

ANNIVERSARIES

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YEVGENIY MIKHAYLOVICH PESHKOV (70TH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (signed to press 13 Apr 87) pp 95-96

[Article by E. Zhilis]

[Text] Yevgeniy Mikhaylovich Peshkov, veteran of Soviet aviation and space medicine, doctor of medical sciences, professor, retired colonel of the medical service, celebrated his 70th birthday on 7 November 1986.

Ye. M. Peshkov was born to a peasant family in Urdmurt ASSR. In 1938, after graduating from the Izhevsk Medical Institute, Yevgeniy Mikhaylovich was called up for duty in the Red Army. In 1939-1940, he particiated in the Soviet-Finnish War, and from 22 June 1941 in the Great Patriotic War as senior physician in an aviation regiment then, from 1944 on, as division physician. Ye. M. Peshkov participated in the battle for Moscow. He was in Konigsberg at the end of the war.

Ye. M. Peshkov has been involved since 1946 in work dealing with aviation physiology, hygiene, toxicology, psychology and ergonomics. He devotes particular attention to problems of altitude physiology (such as effect of hypoxia, barometric pressure changes, positive pressure breathing, means of protection against these factors).

His candidatorial dissertation, which he defended successfully in 1961, dealt with physiological assessment of efficacy of oxygen gear for flight personnel to be used at high altitudes.

Yevgeniy Mikhaylovich devoted much effort to the practical implementation of high-altitude flights, parachute jumps, including record jumps from the stratosphere, problems of safety of abandoning aircraft at high altitudes, and special altitude training of flight personnel.

Ye. M. Peshkov was at the source of space medicine. He participated in the screening of the first Soviet cosmonauts in Air Force units, in refining the specifications and evaluating life-support systems of Vostok and Voskhod spacecraft, space suits, and in preparations for man's first extravehicular activity.

The logical completion of this important period of service and research work of Ye. M. Peshkov was his defense in 1968 of a doctoral dissertation in medical sciences and his confirmation as a professor in 1971 by the USSR High Degree Commission.

After being discharged from the Armed Forces in 1971, Ye. M. Peshkov continued with his fruitful scientific and creative work at the Scientific Research Institute of Civil Aviation, making use of his rich 25-year experience at scientific institutions of the Air Force.

Ye. M. Peshkov has written more than 280 scientific works, including a monograph, textbook and chapters in "Aviatsionnaya meditsina" [Aviation Medicine] textbooks (1960 and 1980). He has often delivered papers at congresses and scientific conferences, including those held abroad.

Ye. M. Peshkov is not only a highly qualified specialist and scientist in the field of aviation and space medicine, but a talented artist. He has painted dozens of pictures, water colors and paintings that have been shown with success at one-man exhibits.

All of his coworkers and disciples appreciate and deeply respect Ye. M. Peshkov as a kind, modest, fair and industrious man and scientist.

Many USSR orders and medals have been bestowed upon Ye. M. Peshkov for his services to his country.

The editorial board of this journal, specialists in aviation and space medicine and technology, friends, comrades, disciples and proponents cordially congratulate Yevgeniy Mikhaylovich Peshkov on his birthday and sincerely wish him good health, happiness and further creative achievements.

ANNOUNCEMENT OF PUBLICATION OF THIRD VOLUME OF COMPREHENSIVE SPECIALIZED BIBLIOGRAPHY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 3, May-Jun 87 (signed to press 13 Apr 87) p 96

[Text] Nauka Publishing House is putting out a retrospective bibliographic index in the first quarter of 1987, "Biomedical and Sociopsychological Problems of Exploration of Space and Regions on Earth With Extreme Living Conditions" (85 sheets [16 printed pages], 4.20 rubles).

This index lists about 10,000 sources referable to 1971-1975. The sources are classified and indexed (more than 130 topical rubrics). The titles of foreign works have been translated into Russian and partially annotated. The index has an ancillary element (index of names and books described under a heading). A wide range of subjects is covered, which are of interest for representatives of different scientific and scientific-practical disciplines: space biology and aerospace medicine; general biology, medicine (theoretical and clinical), industrial engineering and social psychology, as well as for engineers, designers, pedagogues and other specialists.

This bibliographic index is a continuation of three preceding volumes issued by Nauka Publishing House in 1972 and 1977 (references for 1961-1965 and 1966-1970). For subsequent years, the index was published by the USSR State Library imeni V. I. Lenin in the form of annuals (for 1977, 1978, 1979 and 1980).

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